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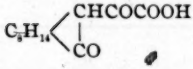
A CONTINUATION OF THE STUDY OF THE ACTION OF AMINES ON CAMPHOROXALIC ACID.

BY J. BISHOP TINGLE AND CHARLES J. ROBINSON.

INTRODUCTION.

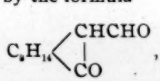
In 1889, J. Bishop Tingle[1] discovered that camphor condenses with ethyl oxalate, in the presence of sodium, the product giving a deep violet-red color with ferric chloride, in alcoholic solution. This is in accord with the work of Claisen and his associates, showing that all ketones, $RCOCH_3$ and $RCOCH_2R'$, condense, in the presence of sodium, with esters, the latter type of ketone yielding the more stable products. All such condensation compounds obtained by Claisen give color reactions with alcoholic ferric chloride. Subsequent investigation[2] of the substance formed by the action of ethyl oxalate on camphor showed that it is the ester of an acid termed *camphoroxalic acid*, which was represented by the formula

[1] Inaug. Diss., Munich, 1889, p. 34.
[2] J. Chem. Soc., **57**, 652 (1890).

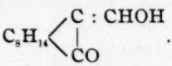


Later, when a general controversy arose as to whether 1,3-diketones are true diketones or unsaturated hydroxy derivatives, a more complete investigation of camphoroxalic acid was undertaken to determine, if possible, whether it has the "keto" or "enol" form, and to study the relative reactivity of the two ketone groups, or the enol and keto groups, the one in the side chain and the other in the ring.

The somewhat analogous compound formed by the action of ethyl formate on camphor, which was at first supposed to have a structure expressed by the formula



has been thoroughly investigated by Bishop, Claisen and Sinclair,[1] and shown to be



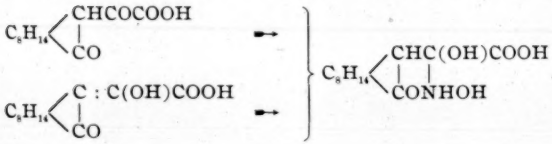
The name oxymethylene camphor was given to the substance by these authors. The work of Bishop Tingle and his associates on camphoroxalic acid[2] has brought to light facts indicating that it likewise has the unsaturated hydroxy structure, though the evidence cannot be considered conclusive. The chief facts hitherto discovered, which bear on the point, are:

1. The production of a stable addition product with hydroxylamine.[3] The stability of the compound is such as to indicate that it is not simply an addition to a carbonyl group. It will be observed that addition to either the diketonic or ketoenolic form would give the same compound, as shown in the formula,

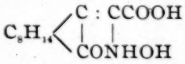
[1] Ann. Chem. (Liebig), **281**, 314.

[2] THIS JOURNAL, **19**, 393 (1897); **20**, 318 (1898); **21**, 248 (1899); **23**, 214 (1900). J. Am. Chem. Soc., **23**, 363 (1901). THIS JOURNAL, **34**, 217 (1905).

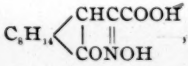
[3] *Ibid.*, **19**, 396, 408.



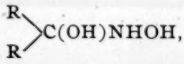
Such a substance might eliminate water in either of two ways, which would result in the formation of the compounds



and



respectively. This latter reaction, however, is simply an expression of the production of an oxime, and it is well known that oxime formation occurs very readily, without its being possible to isolate any intermediate, additive compound, *i. e.*, compounds of the formula

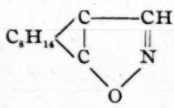


are, in general, highly unstable. The fact that Bishop Tingle's hydroxylamine additive compound was quite stable led him to the conclusion that it resulted from the addition of hydroxylamine to a double linkage in camphoroxalic acid, and, therefore, to regard this acid as being a ketoenolic compound and not a true diketone. This was the first example which had ever been observed of such an addition of hydroxylamine to a double linkage between two carbon atoms. Later, C. Harries[1] and his co-workers found that similar compounds could be obtained from mesityl oxide, phorone, etc.

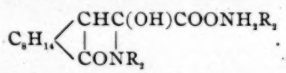
Attempts to dehydrate the camphoroxalic acid hydroxyl-

[1] Ber. d. chem. Ges., 30, 231 2726.

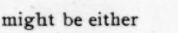
amine product led to the elimination of carbon dioxide and 2 molecules of water, and the formation of camphylisoxazole,[1]



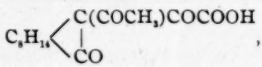
Camphoroxalic acid also forms addition products with diethylamine and dimethylamine[2] of the type,



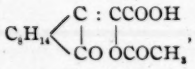
2. With acetic anhydride, a monacetyl derivative,



is produced.[3] This might be either



or

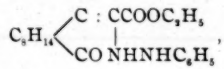


but its formation by the direct action of acetic anhydride on camphoroxalic acid makes the latter structure appear more probable.

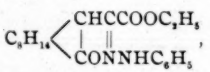
3. Camphoroxalic acid is hydrolyzed by barium hydroxide to camphor and oxalic acid,[4] indicating the existence of a double linkage in the side chain.

4. Ethyl camphoroxalate and phenylhydrazine react[5] to form what appears to be the hydrazide,

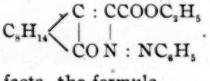
[1] THIS JOURNAL, **19**, 409.
[2] *Ibid.*, **34**, 246.
[3] *Ibid.*, **20**, 324.
[4] *Ibid.*, **20**, 327.
[5] J. Chem. Soc., **87**, 655. THIS JOURNAL, **19**, 402.



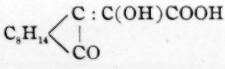
and not the hydrazone,



because, when it is oxidized by mercuric oxide or hydrogen peroxide, it yields a red, crystalline compound,[1]

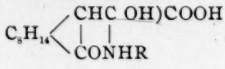


In view of these facts, the formula

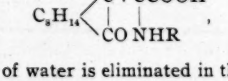


has been tentatively assigned to camphoroxalic acid. The work of Baly and his collaborateurs on the optical properties of enolic and ketonic compounds, of which a review and bibliography has been given recently,[2] lends a considerable amount of support to the conclusion reached, from purely chemical considerations, by the senior author of this paper, that the point of attack in such compounds is the group C : COH and not CO.

The simple reaction products with primary amines are believed to have the general structure,



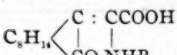
when addition products are formed, and



when a molecule of water is eliminated in the reaction.

[1] THIS JOURNAL, **20**, 338; **21**, 258.
[2] *Ibid.*, **36**, 213.

The hypothesis that compounds



I.

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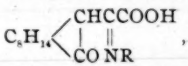
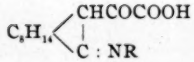


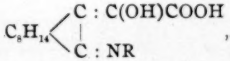
II.

and not



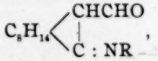
III.

or

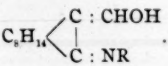


IV.

are produced, is supported by the fact that, when heated, the substances in question give up carbon dioxide, forming neutral products. Compounds of the latter type, where carboxyl is joined to —CO— or >C(OH)—, would not be expected to eliminate carbon dioxide; and, if they did, the products would be aldehydes,



or oxymethylene compounds,



The inactivity and neutrality of the substances actually obtained discredit the possibility of such a structure and leave the choice between the first two formulas. For the reasons discussed above, the former of these, I., is preferred.

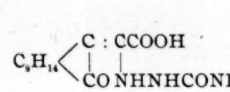
A somewhat extensive investigation of the action of amines, of various types, on camphoroxalic acid has already been made.[1] The present paper contains the results of a continuation of this study. The amines which have been employed are semicarbazine, urea and the methylated ureas, hydrazine, phenylhydrazine and parabromphenylhydrazine. In the course of this investigation, additional evidence indicative of the unsaturated hydroxy structure has been found.

[1] *Vide* Table, THIS JOURNAL, **34**, 236.

THEORETICAL.

The Action of Semicarbazine on Camphoroxalic Acid.

In a preliminary experiment on the action of semicarbazine on camphoroxalic acid, J. Bishop Tingle and Alfred Tingle[1] obtained what appeared to be two isomeric derivatives of the formula



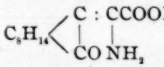
one of which was found to melt at 218° and the other at 209°–210°. The two were separated by the solubility of the former in ether. Subsequently, Bishop Tingle and W. E. Hoffman, Jr.,[2] obtained, under different conditions, a compound of the same formula which, when crystallized from alcohol, melted at 200°, but when crystallized from glacial acetic acid, melted at 209°–210°. Nothing further was done with these substances at that time. To clear up the apparent discrepancy, we have repeated the two earlier experiments and have compared the products carefully, with the result that the supposedly isomeric substances are proved to be identical. The variation in the melting points recorded in the previous work was found to be due to the exhibition, by the compound, of a remarkable sensitiveness not only to the rate of heating, but also, apparently, to small amounts of impurities. Experiments showing the degree of variation due to differences in the rapidity of the heating are tabulated on page 256, the observed melting point varying from 200°.5, when the rate of heating above 190° was 2° per minute, to 217° when the rate was 15° per minute. The presence of a small amount of resinous matter, not sufficiently large to be detected by analyses, was found to render the substance somewhat soluble in ether, which explains the separation into two portions that was effected by Bishop Tingle and A. Tingle.

The compound was designated in the latter of the two papers mentioned above as "semicarbazine camphoformeneaminecar-

[1] THIS JOURNAL, **23**, 224 (1900).

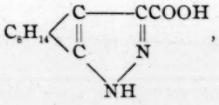
[2] *Ibid.*, **34**, 251 (1905).

boxylic acid." The name *carbamylcamphoformeneaminecarboxylic acid* seems preferable, as showing more clearly the relation to the simpler compound, *camphoformeneaminecarboxylic acid*,



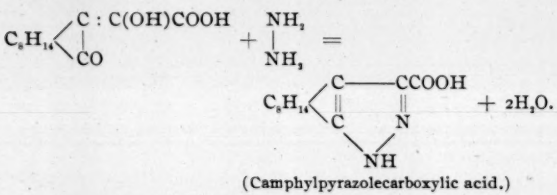
The term "carbamyl" designates satisfactorily the carbamide residue, —$NHCONH_2$, which is present.

When camphoroxalic acid and semicarbazine react at 125°, under pressure, the products are hydrazodicarbonamide, $H_2NCONHNHCONH_2$, and *camphylpyrazolecarboxylic acid*,



both of which are also products of the fusion of carbamylcamphoformeneaminecarboxylic acid (see below). The formation of these compounds, under the conditions employed, is explained by the fact that semicarbazine breaks down under the influence of heat into hydrazodicarbonamide and hydrazine. The hydrazine then interacts with camphoroxalic acid. The reactions may be expressed thus:

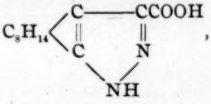
$$\underset{\text{(Semicarbazine.)}}{2NH_2NHCONH_2} = \underset{\text{(Hydrazodicarbonamide.)}}{NH_2CONHNHCONH_2} + H_2NNH_2;$$



(Camphylpyrazolecarboxylic acid.)

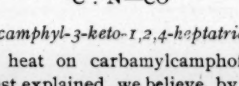
At least three compounds are formed by the fusion of carbamylcamphoformeneaminecarboxylic acid, *viz.*:

1. Hydrazodicarbamide, $NH_2CONHNHCONH_2$, which is insoluble in all the ordinary, neutral, organic solvents, and but slightly soluble in boiling water. It melts at 245° and has been previously obtained from semicarbazine by the elimination of hydrazine.[1] The insoluble compound, melting at 255°, which is mentioned by Bishop Tingle and A. Tingle[2] as being obtained in small amount, was, no doubt, this same substance. It melts at 245° only when heated very slowly.

2. *Camphylpyrazolecarboxylic acid*, C_8H_{14}  ,

which melts at 255°–258°. The fact that the same compound is obtained by the action of hydrazine on camphoroxalic acid confirms the view that it has the above structure.

3. A compound crystallizing from alcohol in yellow needles, which melt at 305°–306°. It has the composition of carbamylcamphoformeneaminecarboxylic acid minus the elements of water and carbon dioxide, and is, without doubt, represented by the formula



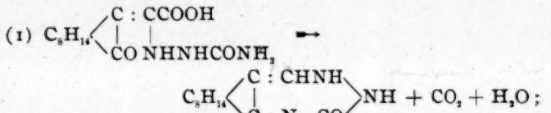
It may be called *camphyl-3-keto-1,2,4-heptatriazine.*

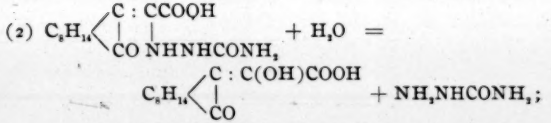
The action of heat on carbamylcamphoformeneaminecarboxylic acid is best explained, we believe, by the following hypothesis: A portion of the compound eliminates water and carbon dioxide and forms the substance melting at 305°–306°. The water thus formed hydrolyzes another portion of the original substance into its components, semicarbazine and camphoroxalic acid. The reaction then proceeds in the same way as when these two substances are heated together under pressure, hydrazine being formed and condensing with camphoroxalic acid. This condensation involves the elimination of water, which hydrolyzes some of the original compound, and

[1] Thiele: Ann. Chem. (Liebig), **270**, 45. Curtius: Ber. d. chem. Ges., **27**, 57.
[2] THIS JOURNAL, **23**, 228.

the greater the extent of the hydrolysis the larger the amount of water subsequently formed. With water present, hydrolysis would be expected to take place more readily than condensation to the 7-membered ring compound, camphylketoheptatriazine. This explains the fact that the latter substance was obtained in very small amount.

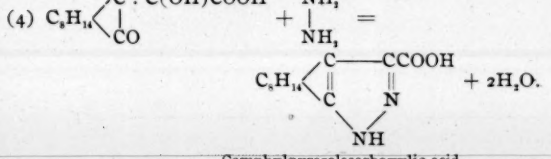
The following equations express the reactions involved :

(1) 

(2) 

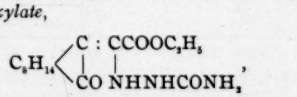
(3) $2NH_2NHCONH_2 = NH_2CONHNHCOH_2N + H_2NNH_2$;

Hydrazodicarbonamide.

(4) 

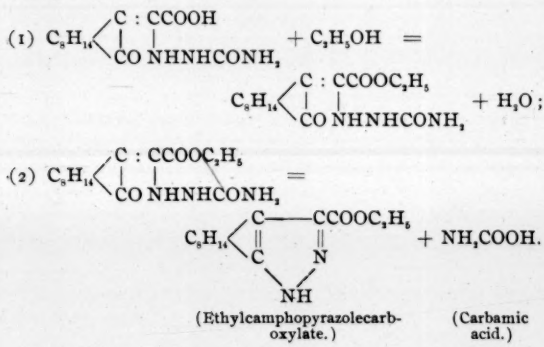
Camphylpyrazolecarboxylic acid.

Experiments were also made on the action of dry hydrogen chloride on carbamylcamphoformeneaminecarboxylic acid, in the presence of absolute alcohol. If the reaction is carried out at about 0°, the primary product is *ethyl carbamylcamphoformeneaminecarboxylate*,



which melts at 191°. The same compound has been described

by Bishop Tingle and A. Tingle,[1] who prepared it by the action of semicarbazine on ethyl camphoroxalate. Their preparation melted at 202°. This difference in melting point is doubtless due to differences in the rapidity of heating, a behavior which is so markedly shown in the case of the acid. When this ester is allowed to stand in the alcoholic hydrochloric acid solution in which it was made it soon decomposes, and ethyl camphylpyrazolecarboxylate is formed, which melts at 91°–92° and crystallizes from ligroin in magnificent, monoclinic, tabular crystals. This ester is strongly basic and forms a stable hydrochloride, that softens at 151° and melts at 156°. Camphylpyrazolecarboxylic acid itself is basic to the extent of dissolving in dilute, aqueous acids, though nearly insoluble in water. The action of hydrochloric acid and alcohol on carbamylcamphoformeneaminecarboxylic acid is represented in the following equations:



(1) $C_8H_{14}\begin{cases} C : CCOOH \\ | \quad | \\ CO\ NHNHCONH_2 \end{cases} + C_2H_5OH = C_8H_{14}\begin{cases} C : CCOOC_2H_5 \\ | \quad | \\ CO\ NHNHCONH_2 \end{cases} + H_2O;$

(2) $C_8H_{14}\begin{cases} C : CCOOC_2H_5 \\ | \quad | \\ CO\ NHNHCONH_2 \end{cases} = C_8H_{14}\begin{cases} C \text{——} CCOOC_2H_5 \\ \| \quad \| \\ C \quad N \\ \quad \diagdown / \\ \quad NH \end{cases} + NH_2COOH.$

(Ethylcamphopyrazolecarboxylate.) (Carbamic acid.)

As carbamic acid, in the presence of hydrochloric acid, would cause the formation of ammonium chloride, which was not observed, it is probable that urethane, $NH_2COOC_2H_5$, was the actual product of the reaction, though its presence was not proved, because our interest was confined chiefly to the other substances involved. The shifting of the double bonds ob-

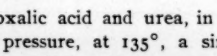
[1] THIS JOURNAL, **23**, 227.

served in the above formula, representing the formation of a pyrazole derivative, requires no comment, as it is well known that such rearrangement occurs generally in pyrazole formation.[1]

The Action of Urea and of the Methylated Ureas on Camphoroxalic Acid.

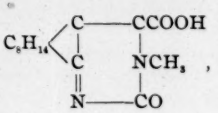
J. Bishop Tingle and W. E. Hoffman, Jr.,[2] found that when urea and camphoroxalic acid are heated together no compound could be isolated from the tarry reaction product. Under different conditions, we have succeeded in obtaining a urea derivative and also derivatives of methylurea and the symmetrical dimethylurea.

When camphoroxalic acid and urea, in alcoholic solution, are heated under pressure, at 135°, a simple condensation takes place and *formamidylcamphoformeneaminecarboxylic acid,*



is formed. It melts at 192°–194°.

When camphoroxalic acid and methylurea are heated together, without a solvent, or when an alcoholic solution of these substances is heated under pressure, at 100°, condensation takes place with elimination of 2 molecules of water, the product being *1-methyl-2-keto-4,5-camphylmetadiazine-6-carboxylic acid,*

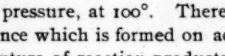


which melts at 154° and is deposited from ethyl acetate solution in slightly yellow, long, prismatic crystals. The fact that a secondary amine group condenses with camphoroxalic acid is significant, and could scarcely be explained on any other basis than that of the unsaturated hydroxy structure of the

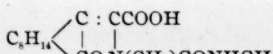
[1] Knorr: Ann. Chem. (Liebig), 279, 188.
[2] *Loc. cit.*

latter. It is also noteworthy that the condensation takes place much more readily than with urea itself. This is, perhaps, to be attributed to the more basic character of an alkylated amine as compared with the simpler compound. The influence of methyl in one of the amine groups evidently extends also to the second amine, for we find it entering into reaction, whereas, in the case of urea, the second amine group is unaffected under similar conditions.

Symmetrical dimethylurea and camphoroxalic acid react readily when a methyl alcoholic solution of the two substances is heated, under pressure, at 100°. There is difficulty in isolating the substance which is formed on account of the tarry nature of the mixture of reaction products; finally, however, a small quantity of a compound was obtained which melted at 104°–105°. A larger amount of a second compound, melting at 77°–78°, was also isolated; it proved to be *methylcamphoformeneaminecarboxylic acid*,



This may have been produced either by the action of methylamine resulting from the decomposition of a part of the dimethylurea during the heating, or, on the other hand, a dimethylurea derivative of camphoroxalic acid, such as



may have been first formed, and then hydrolyzed to the methylamine compound by the treatment employed in the attempts to isolate the product. The fact that the odor of methylamine was not at first perceptible, but developed during this process, and the further fact that a small amount of an unknown compound actually separated, makes the second hypothesis appear the more probable. Hydrolysis of the methylurea compound formulated above would, presumably, yield carbon dioxide, methylamine and methylcamphoformenecarboxylic acid. The latter substance, which, as already mentioned, was

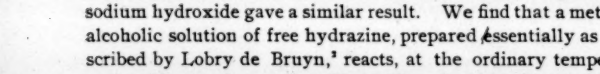
actually obtained, is the missing member of the series of methylamine derivatives of camphoroxalic acid which Bishop Tingle and W. E. Hoffman, Jr.,[1] were unable to prepare under the conditions employed by them.

All attempts to get condensation products of camphoroxalic acid and the unsymmetrical dimethylurea were unsuccessful.

The Action of Hydrazine on Camphoroxalic Acid.

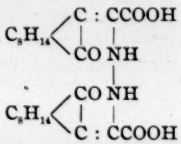
Bishop Tingle and W. E. Hoffman, Jr.,[2] failed to obtain any reaction when camphoroxalic acid, hydrazine hydrochloride and sodium hydroxide were dissolved in alcohol and heated on the water-bath. The use of barium hydroxide in place of sodium hydroxide gave a similar result. We find that a methyl alcoholic solution of free hydrazine, prepared essentially as described by Lobry de Bruyn,[3] reacts, at the ordinary temperature, with camphoroxalic acid, yielding three products :

1. *Hydrazine camphoroxalate,*



when in a dry condition, this is a stable salt. It begins to decompose only at 186°, but in solution it dissociates when gently warmed, and the liberated hydrazine condenses with 2 molecules of the acid. Aqueous sodium carbonate also decomposes it, and acidification yields the condensation product, bicamphoformeneaminecarboxylic acid.

2. *Biscamphoformeneaminecarboxylic acid,*



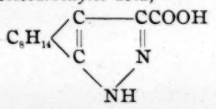
is obtained by the condensation of 1 molecule of hydrazine with 2 molecules of camphoroxalic acid. It is a yellow sub-

[1] This Journal, 34, 249.
[2] Rec. Trav. Chim., 13, 433.

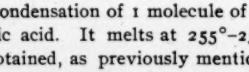
stance which decomposes, without complete fusion, at 150°–155°.

When crystallized from methyl alcohol, it takes up 2 molecules of the alcohol, which are not readily expelled. The crystallized product has a different appearance and different solubilities from the dried substance, and it begins to decompose at 137°. It appears, therefore, that the 2 molecules of solvent are held in closer combination than is usually the case with solvent of crystallization. This is a strong indication of unsaturation in the molecule.

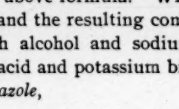
3. *Camphylpyrazolecarboxylic acid,*



is formed by the condensation of 1 molecule of hydrazine with 1 of camphoroxalic acid. It melts at 255°–258°. The same compound was obtained, as previously mentioned, from carbamylcamphoformeneaminecarboxylic acid,

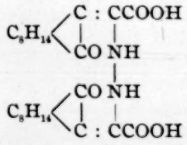


when it is decomposed by heat; its ester was formed by the action of dry hydrochloric acid gas on the same compound, in absolute alcoholic solution. From the facts detailed below, there can be little doubt that this substance is a pyrazole derivative as represented in the above formula. When fused, carbon dioxide is eliminated, and the resulting compound gives a violet color if reduced with alcohol and sodium, and subsequently oxidized with nitric acid and potassium bichromate, indicating that it is *camphylpyrazole,*



This substance remains unmelted up to temperatures as high as 288°.

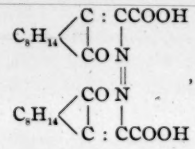
The behavior of biscamphoformeneaminecarboxylic acid,



at high temperatures was then investigated. It was found that at least 3 substances are formed, but a complete study of them has not, as yet, been made. The details of the separation of these compounds from the fused material are given in the experimental part, p. 273; eventually the following products were isolated:

1. A *compound*, $C_{24}H_{30}O_6N_2$, which differs from the parent material, $C_{24}H_{32}O_6N_2$, by containing 2 atoms of hydrogen less. This substance crystallizes from ethyl acetate in nodular clusters of fine needles, which have a light yellow color and melt at 222°–223°. The body is an acid, but nothing further was learned regarding its constitution.

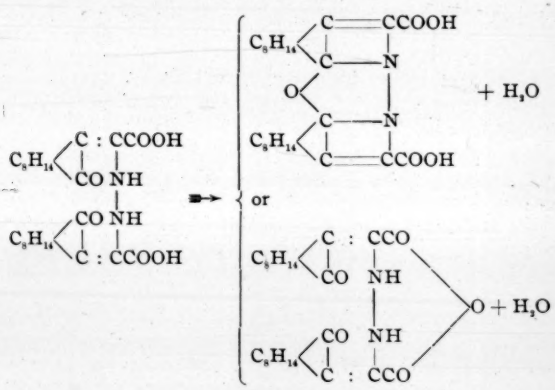
2. A *compound*, which is also an acid and is isomeric with the preceding substance. It melts at 232° and has a dull yellow color, but is usually tinged with red, and its solutions, on standing, become red and deposit red crystals which have practically the same melting point as the yellow substance. The colored material may, perhaps, have an azo structure, such as



but as the pure compound is only slightly colored, this particular formula would hardly apply to it.

3. A *compound*, the analysis of which gave the formula

$C_{24}H_{30}O_6N_2$. The substance was, however, obtained in such small quantity that the results require confirmation. If this formula should prove to be correct, the substance is formed from the parent compound, biscamphoformeneaminecarboxylic acid, by elimination of water, thus:

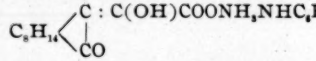


So far as our limited knowledge permits the expression of an opinion, we incline to favor the first of these formulas. The substance crystallizes from ethyl acetate in light yellow, translucent prisms, which melt at 221°. The quantity of material available was too small to permit a more thorough examination of this compound at present, but in the immediate future it is planned to continue the investigation of all three of these substances in this laboratory.

The Action of Phenylhydrazine on Camphoroxalic Acid.

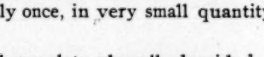
In view of the results which were obtained by the action of hydrazine on camphoroxalic acid, it appeared desirable to extend the investigation to the action of phenylhydrazine on camphoroxalic acid. In the course of some work on the subject, Bishop Tingle had prepared the following derivatives of this base:

1. Phenylhydrazine camphoroxalate (?),[1]



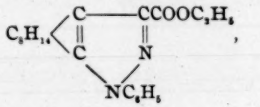
melting at 214°–215°, with previous darkening. This had been prepared only once, in very small quantity, and had not been analyzed.

2. Ethyl camphoroxalate phenylhydrazide,[2]



prepared by condensing ethyl camphoroxalate and phenylhydrazine. It melts at 212°. The corresponding methyl ester was also obtained from methyl camphoroxalate.[3]

3. Ethyl camphylphenylpyrazolecarboxylate,[4] m. p. 114°,



and the corresponding methyl ester,[5] m. p. 80°.5–81°.5, were prepared by the condensation of the respective phenylhydrazides with dehydrating agents.

4. Camphylphenylpyrazolecarboxylic acid,[6] m. p. 197°, was derived by hydrolysis from both of the preceding esters.

In the course of the present investigation we have obtained camphylphenylpyrazolecarboxylic acid directly from camphoroxalic acid. In addition, it has been found possible to isolate a new compound, the primary reaction product when camphoroxalic acid, or potassium camphoroxalate and phenylhydrazine are brought together at the ordinary temperature. This is the *addition compound*,

[1] THIS JOURNAL, **20**, 328 (1898).

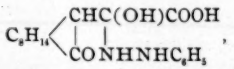
[2] J. Chem. Soc., **57**, 655 (1890). THIS JOURNAL, **19**, 402 (1897); **20**, 338 (1898); **21**, 258 (1899).

[3] *Ibid.*, **20**, 335.

[4] *Ibid.*, **19**, 403.

[5] *Ibid.*, **20**, 336.

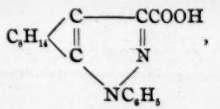
[6] *Ibid.*, **19**, 405; **20**, 336.



which melts at 120° and crystallizes in very fine, yellow needles. It is quite stable, and can be boiled in weakly dissociating solvents like ether, chloroform and benzene without decomposition. Over sulphuric acid, in a vacuum desiccator, it remained unchanged after standing for 2 months. The possibility of the compound being a salt is excluded by its formation from potassium camphoroxalate.

The stability of this addition compound is another strong argument in favor of the unsaturated hydroxy structure for camphoroxalic acid. A few addition products of phenylhydrazine with true ketones have been isolated; several esters of oxalacetic acid[1] and of dioxysuccinic acid[2] form such derivatives when the reaction takes place at a low temperature, but otherwise, by the elimination of water, the reaction proceeds to the formation of phenylhydrazones. The addition compounds of the esters of dioxysuccinic acid lose water when left standing either alone, or covered with ether or alcohol. The corresponding compound with ethyl oxalacetate is changed to the hydrazone by warming its solutions; and when it was allowed to remain for 12 days, in a vacuum desiccator, over sulphuric acid, it was quantitatively transformed to the phenylhydrazone. It is evident, therefore, that the addition compound with camphoroxalic acid is not to be classed with the addition products of true ketones and phenylhydrazine.

This compound, after being boiled for some time with alcohol, or when fused, condenses to camphylphenylpyrazolecarboxylic acid,

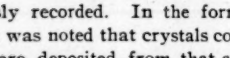


the melting point of which was observed to be 196° instead of

[1] W. Wislicenus and Max Scheidt: Ber. d. chem. Ges., **24**, 3006 (1891).
[2] Anschütz and Pauly: *Ibid.*, **28**, 66 (1895).

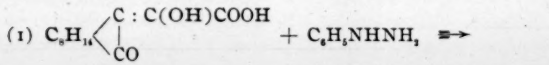
197°, as previously recorded. In the former description of this substance,[1] it was noted that crystals containing 0.5 molecule of benzene were deposited from that solvent. It is now found that the compound crystallizes very readily from alcohol with 1 molecule of alcohol of crystallization.

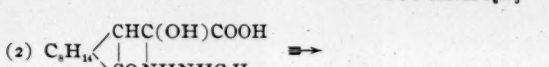
Attempts to eliminate 1 molecule of water from the addition compound, so as to form the phenylhydrazide of camphoroxalic acid,

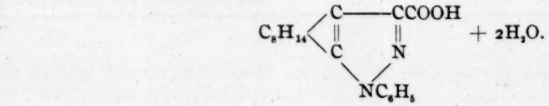


were unavailing. The condensation always went further, and 2 molecules of water were eliminated, giving the pyrazole derivative. Unsuccessful attempts were also made to obtain the "phenylhydrazine camphoroxalate" previously described. It appears, therefore, that the formation of this substance, whatever be its nature, depends on some slight variations of experimental conditions which were not noted at the time when the original experiment was carried out, and which we have been unable to reproduce.

The action of phenylhydrazine on camphoroxalic acid may be expressed by the equations:







[1] *Loc. cit.*

The Action of Parabromphenylhydrazine on Camphoroxalic Acid.

We extended the investigation so as to include a study of the action of parabromphenylhydrazine on camphoroxalic acid, partly in order to ascertain the effect of the negative bromine atom on the properties and stability of the condensation products, and partly in the hope of preparing some substances belonging to types which were not represented by the compounds which we had succeeded in isolating from hydrazine and from phenylhydrazine. As the result of our experiments, the following 5 derivatives have been obtained:

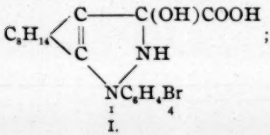
1. *An addition compound,*

$$C_8H_{14}\begin{cases}\text{CHC(OH)COOH}\\ \text{CO}\quad\text{NHNHC}_6\overset{4}{\text{H}}_4\overset{1}{\text{Br}}\end{cases},$$

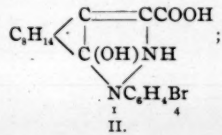
corresponding to the addition compound obtained with phenylhydrazine. It is formed, together with the next compound described, whenever parabromphenylhydrazine and camphoroxalic acid are brought together in solution, at the ordinary temperature, and the reaction proceeds in the same way when the solution is heated. The substance melts at 149° and crystallizes in fine, yellow needles—a deeper yellow than that of the corresponding phenylhydrazine derivative. The stability of the compound is such that it is unaffected by heating with acetic anhydride, on the water-bath, for an hour. No products formed by the addition of amines to aldehyde or ketone groups have shown a comparable degree of stability, and although the facts can best be explained by supposing that the addition has taken place at the double linkage in the group >C : COH— (*vide* pp. 225, 227), yet it does not account for this stability.

2. The second compound, which is always obtained with the preceding one, melts at 172°. In some experiments, compound number 1 separated first from the solvent, and then the second substance; in other experiments the order of separation was exactly reversed, and sometimes both compounds came down simultaneously. We were unable to ascertain exactly what conditions determine which substance shall precipitate first. This behavior furnishes another illustration of the considera-

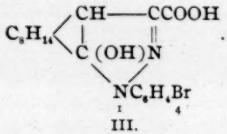
ble differences in results which are brought about by relatively minute variation in the experimental conditions, a fact that must be constantly kept in mind in dealing with substances belonging to this class. The compound under discussion differs in composition from the additive compound by 1 molecule of water; but in the fact that it is not vigorously attacked by concentrated nitric acid, and in its crystallizing power, it resembles the pyrazole derivatives rather than the hydrazides. It appears, therefore, to have the constitution expressed by one of the following formulas:



I.

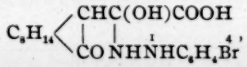


II.



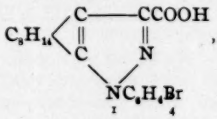
III.

The addition compound being



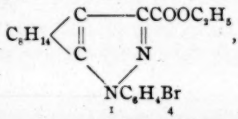
it seems most probable to suppose that the second nitrogen atom combines with the carbonyl of the camphor ring, with the elimination of water, which would then give the structure represented in Formula I. Further work will be necessary to decide this point.

3. *Camphylparabromphenylpyrazolecarboxylic acid*,

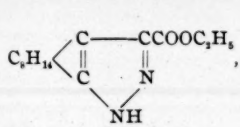


melting at 215°, is formed when either of the two compounds just described is fused. It is interesting to note that the addition compound loses 2 molecules of water at once, instead of first losing 1 molecule and forming the intermediate product, (2) although the latter is a very stable substance. The same conduct is characteristic of the addition compound with phenylhydrazine. This compound (m. p. 215°) is colorless, and crystallizes from benzene in nodular clusters of minute needles.

4. *Ethyl camphylparabromphenylpyrazolecarboxylate,*

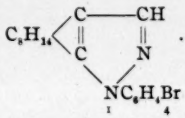


was obtained by treating the addition compound, m. p. 149°, with absolute alcohol, saturated with dry hydrochloric acid, at 0°. It melts at 107° and crystallizes from acetone in magnificent, triclinic crystals. In contrast to ethyl camphylpyrazolecarboxylate,



this substance shows no basic properties.[1]

5. A compound, not analyzed, which is probably *camphylparabromphenylpyrazole,*



It is formed by fusing camphylparabromphenylpyrazolecarboxylic acid, carbon dioxide being eliminated. The substance is extremely soluble in all the ordinary organic menstrua, and remains as a gummy mass after the solvent has evaporated

[1] *Vide* p. 233.

spontaneously. It was not found possible to purify the body sufficiently for analysis.

Of these five compounds, it is seen that the first two have an important bearing on the structure of camphoroxalic acid and tend to confirm the unsaturated hydroxy formula.

The Hydration Product of Camphoroxalic Acid.

In order to obtain, if possible, further evidence of the unsaturated character of camphoroxalic acid, an investigation was undertaken of the hydration product obtained by Bishop & Tingle[1] when the acid is heated, under pressure, with aqueous solutions of mineral acids. The substance in question has the composition of camphoroxalic acid plus 2 molecules of water and, in alcoholic solution, gives a blue color with ferric chloride. It was prepared by the use of sulphuric acid as described in the earlier paper[2], but difficulty was experienced in working with it because of its extremely ready reversion to camphoroxalic acid. It was found that 4 equivalents of sodium carbonate are required to neutralize it, which indicates that there are 3 hydroxyls present, besides the carboxyl. This confirms the analysis previously published[3] and indicates that the water is not present as water of crystallization.

With aniline and semicarbazine, respectively, at the ordinary temperature, products were formed which were found to be identical with the corresponding camphoroxalic acid derivatives, but with hydroxylamine, what appears to be a new substance was obtained which melts at 181°–182°, but has not been investigated. The work was not pushed further because of the difficulty of obtaining the pure hydrated acid in quantity.

Summary of the Points Bearing on the Structure of Camphoroxalic Acid.

In the introduction to this paper, several facts were mentioned[4] as having contributed to the belief that camphoroxalic

[1] THIS JOURNAL, **20**, 329 (1898).
[2] *Loc. cit.*
[3] *Loc. cit.*
[4] *Vide* p. 224.

acid is not a true diketone, but an unsaturated hydroxy ketone, *viz.*:

1. The production of a stable addition product with hydroxylamine; and also the formation of addition products with diethylamine and dimethylamine.

2. The formation of a monacetyl derivative with acetic anhydride.

3. The hydrolysis with barium hydroxide, yielding oxalic acid and camphor.

4. The production of a phenylhydrazide instead of a phenylhydrazone.

In this investigation the following additional facts have been discovered which tend to confirm the unsaturated hydroxy structure:

1. Methylurea reacts readily with camphoroxalic acid—much more readily than does urea itself. Both the primary and secondary amine groups enter into the condensation, forming a metadiazine derivative. The condensation of a secondary amine group with a ketone is less easily explained than its reaction with the group $>C:C(OH)-$. Symmetrical dimethylurea also appears to react with camphoroxalic acid, and Mr. Williams, in this laboratory, has prepared a condensation product with symmetrical acetylphenylhydrazine, both of which facts argue for the enolic form of the acid.

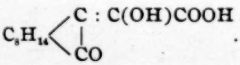
2. Camphoroxalic acid yields an addition product with phenylhydrazine, which is much more stable than any addition products from true ketones which have ever been observed hitherto.

3. Parabromphenylhydrazine yields a still more stable addition product.

4. With parabromphenylhydrazine a ring compound is obtained in which both the keto (or the keto and the enolic) groups have reacted, but with the elimination of only 1 molecule of water. These last three facts are entirely beyond the range of common experience with ketones, and must be explained by the enolic hypothesis.

The general result of this investigation has been, therefore,

to strengthen the view that camphoroxalic acid should be represented by the formula

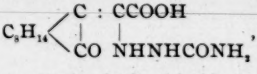


The various derivatives thus far obtained by the action of the amines studied in this investigation are represented in the following table, pp. 249–253, and the relations existing between them are indicated.

EXPERIMENTAL.

In the preparation of camphoroxalic acid, one or two minor changes were made in the method as described by Bishop Tingle and W. E. Hoffman, Jr.[1] Instead of 400 cc. of petroleum ether for each portion of the reacting substances, 350 cc. were used, and satisfactory results were obtained. In distilling the petroleum ether from the reaction product, sufficiently diminished pressure was employed to keep the temperature of the liquid in the flask below 110° to the end of the operation. No difficulty was experienced in accomplishing this with the ordinary water suction-pump. Otherwise the substance was prepared exactly as described by the authors mentioned.

The Supposedly Isomeric Semicarbazine Derivatives of Camphoroxalic Acid.—In the course of some earlier work on camphoroxalic acid derivatives, J. Bishop Tingle and Alfred Tingle[2] found what appeared to be two isomeric compounds,

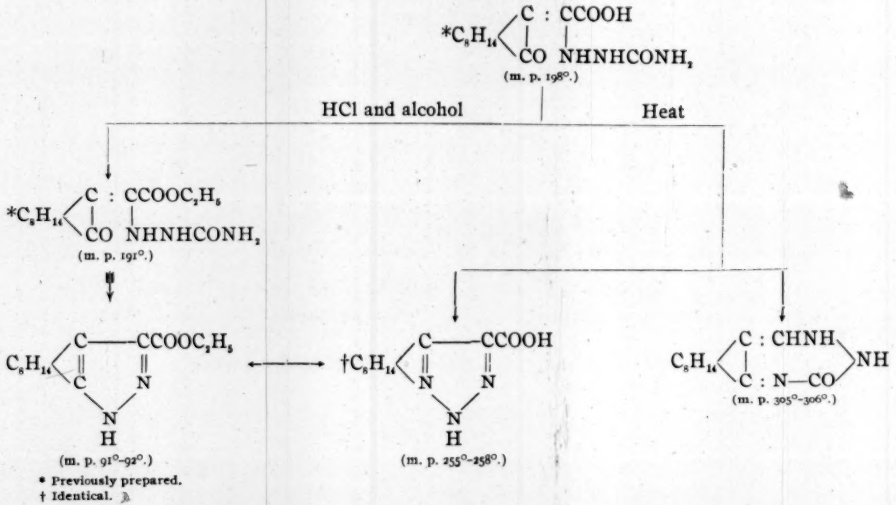


formed when semicarbazine hydrochloride (2 mols.), camphoroxalic acid (1 mol.) and potassium hydroxide (3 mol.) were heated at 100°, for 4 hours, in a closed tube, with alcohol as a solvent. One substance was described as soluble in ether, and melted at 218° when crystallized from acetone; the other was insoluble in all neutral, organic media, and melted at 209°–210° when crystallized from glacial acetic acid. In a later

[1] THIS JOURNAL, **34**, 235 (1905).
[2] *Ibid.*, **23**, 224 (1900).

Table I.—Derivatives of Camphoroxalic Acid with :

SEMICARBAZINE.



* Previously prepared.
† Identical.

Table I.—Derivatives of Camphoroxalic Acid with (Continued):

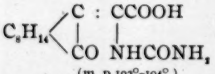
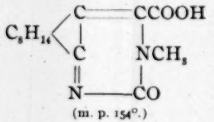
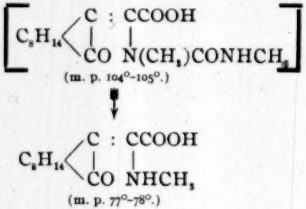
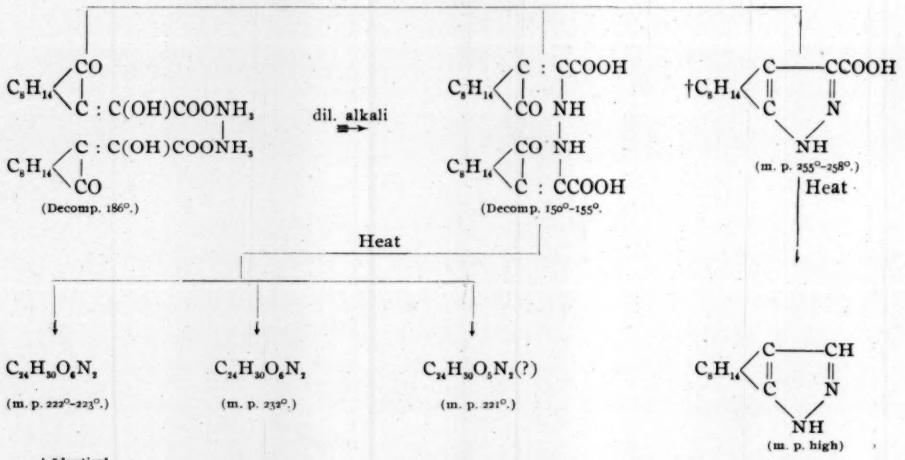
UREA.	METHYLUREA.	SYM. DIMETHYLUREA.	UNSYM. DIMETHYLUREA.
 (m. p. 192°–194°.)	 (m. p. 154°.)	 (m. p. 104°–105°.) (m. p. 77°–78°.)	———

Table I.—Derivatives of Camphoroxalic Acid with (Continued):

HYDRAZINE.



† Identical.

paper, J. Bishop Tingle and W. E. Hoffman, Jr.,[1] described two substances obtained by boiling on the water-bath an aqueous-alcoholic solution of semicarbazine hydrochloride (2 mols.), potassium acetate (2 mols.) and camphoroxalic acid (1 mol.). Evaporation of most of the alcohol and the addition of water precipitated a substance which could be crystallized from alcohol and which melted at 200°. It had the same composition as the two compounds referred to above. When this substance was crystallized from glacial acetic acid its melting point was found to be 209°–210°, and it was, therefore, supposed to be identical with the "insoluble compound" described in the earlier paper. In both these papers the experiments were expressly stated to be only of a preliminary nature.

We have made a further investigation of the action of semicarbazine on camphoroxalic acid, in order to try to throw light on this supposed isomerism. First the experiment in which the substances reacted in a closed tube was carried out, and the product treated exactly as described by Bishop Tingle and A. Tingle. After evaporation of the alcohol and acidification of the residue, the precipitate was washed repeatedly with ether and the filtrate extracted three times with fresh portions of the same solvent. The substance left by evaporation of the combined ethereal residues was crystallized twice from acetone, and the material left undissolved by ether was crystallized twice from glacial acetic acid, by the addition of alcohol. The melting-points of these two portions of the reaction product were then compared by determining both simultaneously, in tubes attached to the same thermometer. They melted at exactly the same temperature.

The reaction was next carried out in the manner described by Tingle and Hoffman. Potassium acetate was used to liberate the semicarbazine from its hydrochloride, and the mixed components were boiled on the water-bath until the alcohol was almost entirely evaporated. The crystalline substance, obtained by dilution with water, was recrystallized from alcohol and a part of the recrystallized product was boiled with glacial acetic acid for a few minutes and crystallized by the addition

[1] This Journal, **34**, 251 (1905).

of alcohol. The two portions, one from alcohol and one from acetic acid, were found to melt at exactly the same temperature when heated simultaneously. Boiling vigorously in glacial acetic acid for half an hour did not change the substance. The compound, when dissolved in potassium carbonate solution and precipitated by acid, appeared in a gelatinous form, but this, when filtered and dried, still melted at the same temperature as before. It was also found that the two substances obtained by the method first described, and the two obtained by this second process, showed identical melting points when any two of them were compared by heating simultaneously in tubes attached to the same thermometer. Furthermore, a mixture of any two of them, when tested in the same manner with each one of the unmixed substances, showed no change in melting point. Samples of the compounds prepared by Bishop Tingle and A. Tingle and by Bishop Tingle and Hoffman were available; therefore the question was further tested by making an exhaustive comparison of these with each other, and with the newly prepared material. With every possible mixture of equal parts of any two of them, the results, in every case, showed that all the preparations were identical.

In the work described above, it was found that the observed melting point varied widely with the rate of heating, and to make accurate comparisons was possible only by attaching 2 capillaries, containing portions of the two substances to be compared, to the thermometer bulb at the same time, and heating them together. The following data on the variation of the melting-point of this semicarbazine derivative were obtained by experiment. In all cases, the capillary containing the substance was placed in the melting point bulb when the thermometer registered 190°, and the heating was begun at once. Capillaries of about the same size were used in all these determinations.

Table II.

	Rate of rise (above 190°).	Time required.	Observed melting point.
1	2° per minute	5 min. 15 sec.	200°.5
2	4° " "	4 "	205°.5
3	6° " "	3 "	208°
4	8° " "	2 " 20 "	209°
5	9° " "	2 " 10 "	209°.5
6	15° " "	1 " 5 "	217°

It was subsequently found that if the substance is heated still more slowly, it melts at 198°; but it will not melt lower than that even with an hour's heating. This must, therefore, be considered the true decomposing temperature of the compound. From the results obtained by Bishop Tingle and A. Tingle,[1] it is evident that an unusual sensitiveness of this compound to slight traces of impurity is a further factor in the variation in melting point.

The substance is rather sparingly soluble in both alcohol and acetone and, when pure, it is practically insoluble in ether. When the crude reaction product is washed with ether, however, the resinous matter which is present appears to render the compound somewhat soluble, which explains why some of it was found in the ethereal washings. The varying data previously recorded in regard to both the solubility and the melting point of this substance are, therefore, satisfactorily explained.

Many other derivatives of camphoroxalic acid, especially those with high melting-points, show a sensitiveness to the rate of heating similar to that described above, though not usually in so marked a degree. The melting points recorded throughout this work are those observed with very slow heating.

The Action of Heat on Carbamylcamphoformeneaminecarboxylic Acid, $C_8H_{14}\begin{cases} C : CCOOH \\ | \quad | \\ CO\ NHNHCONH_2 \end{cases}$.

As stated in the theoretical portion of this paper, at least 3 compounds are formed by heating carbamylcamphoformeneaminecarboxylic acid, *viz.*:

[1] *Loc. cit.*

1. Hydrazodicarbonamide, m. p. 245°.
2. Camphylpyrazolecarboxylic acid, m. p. 255°–258°.
3. Camphyl-3-keto-1,2,4-heptatriazine, m. p. 305°–306°.

The experiments were carried out as follows:

The substance was heated in test tubes of 15 mm. diameter, about 3 grams being contained in each. The test tubes were placed in a sulphuric acid-bath in which a thermometer was suspended. It was found that, even when the temperature was raised very slowly, no fusion took place below 198°. After the mass began to fuse the temperature was kept between 196° and 200°, for 20 minutes. Water and carbon dioxide were evolved, neither of them abundantly.

The cooled mass was hard and brittle, with a reddish-brown color and a nitrile-like odor. The odor of camphor was also slightly perceptible. The separation of the products of reaction involved considerable difficulty, but finally the following method was found to be satisfactory:

The powdered mass is treated with cold acetone, filtered and washed repeatedly with acetone. The undissolved portion is then boiled several times with portions of alcohol until the substance still left undissolved is colorless. It is then filtered and washed with alcohol. The white, insoluble substance melts at 235°. The alcohol filtrates are collected and evaporated to crystallization, yielding a yellow substance melting at 305°–306°. It is purified by boiling with acetone, filtering and washing with acetone. The undissolved material is then recrystallized from alcohol until pure. All the acetone filtrates from the first treatment of the fused material, as well as from the operations just described, are brought together, and the acetone evaporated. A tarry mass remains; by careful treatment with a small amount of cold acetone, much of the tarry matter can be dissolved, leaving a granular substance which is further purified by filtering and washing with a little acetone. Two or three recrystallizations from acetone give a nearly pure, colorless body, crystallizing in small prisms. When pure, it softens at about 250°, shows marked decomposition at 255° and fuses completely at 258°. More of this

compound can be recovered from the tarry mass by treating it with sodium carbonate solution, filtering and acidifying.

Two of these substances were also obtained when camphoroxalic acid and semicarbazine were allowed to react at 125°, under pressure. Eight and eight-tenths grams of camphoroxalic acid (1 mol.), 8.8 grams of semicarbazine hydrochloride (2 mols.) and 6.8 grams of potassium hydroxide (3 mols.) were placed in a bomb with 100 cc. of 95 per cent alcohol, and heated for 6 hours, at 124°–126°. The alcohol was then evaporated and water added. A part of the solid remained undissolved. It was dark from the presence of impurities, but boiling with alcohol removed the color and the compound, being insoluble, was left in nearly pure condition. It was found to be identical with the substance melting at 245°, which was obtained by the fusion of the original semicarbazine derivative. The alcohol solution of the dark impurities was decolorized with animal charcoal, and the alcohol boiled off. A small amount of thick, yellow oil was left which gave a brownish-red color with ferric chloride, in alcoholic solution. It was not further investigated. The aqueous filtrate from the insoluble substance, m. p. 245°, gave, on acidification, a white, finely crystalline substance which softened at 250° and melted at 255°–258°. It was shown by the mixture test to be identical with the compound of the same melting point which was obtained amongst the products of fusion of the semicarbazine compound.

1. *Hydrazodicarbonamide.*—The compound melting at 245° is soluble in 150–200 parts of boiling water and, on cooling, crystallizes in very thin plates. Two recrystallizations suffice for purification. The substance is insoluble in all the ordinary organic media, and dilute acids and alkalies have no effect upon it. It readily reduces an ammoniacal solution of silver nitrate. Analysis :

I. 0.2290 gram substance gave 0.1705 gram CO_2 and 0.1091 gram H_2O.

II. 0.0933 gram substance gave 37.9 cc. N_2 at 18° and 764 mm.

	Calculated for $C_3H_4O_2N_4$.	Found.
C	20.34	20.30
H	5.12	5.33
N	47.45	47.17

The compound is, undoubtedly, hydrazodicarbonamide, which is formed by heating semicarbazine, elimination of hydrazine taking place.

2. Camphylpyrazolecarboxylic Acid.——The substance melting at 255°–258° is slightly soluble in boiling water, but insoluble in cold. It dissolves in a solution of sodium carbonate and is precipitated by acid, but dissolves in excess of acid. Crystals of the substance are readily soluble in cold, dilute acids, showing that it has basic as well as acidic properties. In alcohol it is extremely soluble, but is readily recrystallized from acetone. The crystals are thick, colorless, prismatic forms, usually aggregated into clusters. Analysis:

I. 0.1844 gram substance gave 0.4478 gram CO_2 and 0.0894 gram H_2O.

II. 0.2330 gram substance gave 0.5615 gram CO_2 and 0.1575 gram H_2O.

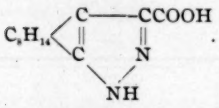
III. 0.1957 gram substance gave 0.4715 gram CO_2 and 0.1387 gram H_2O.

IV. 0.1165 gram substance gave 13.5 cc. N_2 at 25° and 761 mm.

V. 0.1760 gram substance gave 20.1 cc. N_2 at 22° and 755 mm.

	Calculated for $C_{13}H_{16}O_2N_2$.	Found. I.	II.	III.	IV.	V.
C	65.45	66.23	65.73	65.71	. .	. .
H	7.27	6.83	7.56	7.92	. .	. .
N	12.73	. .	. .	. .	12.94	12.83

The same compound was subsequently obtained by the interaction of hydrazine and camphoroxalic acid, and this fact, taken in conjunction with its properties, makes it practically certain that the substance is camphylpyrazolecarboxylic acid,



Its basic properties are attributable to the pyrazole residue.

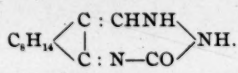
3. Camphyl-3-keto-1,2,4-heptatriazine.—The yellow substance, melting at 305°–306°, which was obtained from the fused material, crystallizes from alcohol in small prisms. The compound does not dissolve in a solution of sodium carbonate. It is fairly soluble in alcohol and difficultly soluble in ether, acetone, benzene and ligroin. From 12 grams of the semicarbazine compound, less than 1 gram of this substance was obtained, and this quantity was reduced to only about 250 milligrams in the process of purification. Hence no extensive study of its properties could be made. Analysis:

I. 0.1630 gram substance gave 0.3917 gram CO_2 and 0.1160 gram H_2O.

II. 0.0902 gram substance gave 15.2 cc. N_2 at 19° and 750 mm.

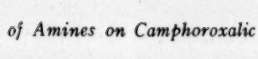
	Calculated for $C_{13}H_{17}ON_3$.	Found. I.	II.
C	65.75	65.54	. .
H	7.76	7.96	. .
N	19.18	. .	19.11

The compound has the composition of carbamylcamphoformeneaminecarboxylic acid minus the elements of water and carbon dioxide, and hence is assumed to have the structure represented by the formula



The manner of the formation of these three substances from carbamylcamphoformenecarboxylic acid, by the action of heat, is explained in the theoretical part of this paper (*vide* p. 230).

The Action of Hydrochloric Acid and Alcohol on Carbamylcamphoformeneaminecarboxylic Acid,



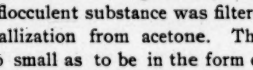
The carbamyl derivative was mixed in a flask with absolute alcohol and dry hydrochloric acid gas was led into saturation, the temperature being kept low by immersing the flask in ice-water. A flocculent, white substance began to be formed some time before saturation was reached, and eventually appeared in considerable quantity; but when the saturated solution was allowed to stand, even at o°, it gradually disappeared.

Some of this flocculent substance was filtered out and purified by recrystallization from acetone. The crystals were colorless, but so small as to be in the form of powder. The compound is readily soluble in hot alcohol, but sparingly in cold. It easily dissolves in ether and chloroform, is sparingly soluble in benzene, and insoluble in ligroin. It does not dissolve in sodium carbonate solution. The substance melts at 191°.

Analysis: 0.0843 gram substance gave 0.1798 gram CO_2 and 0.0597 gram H_2O.

	Calculated for $C_{12}H_{22}O_4N_2$.	Found.
C	58.25	58.17
H	7.44	7.92

The analysis shows the compound to be *ethyl carbamylcamphoformeneaminecarboxylate,*,



which has been previously prepared by Bishop Tingle and A. Tingle, as mentioned in the first part of this paper.

The clear, alcoholic solution, saturated with hydrochloric acid, was poured into a large volume of dilute sodium carbonate solution. An emulsion was formed, but on standing over night the emulsified substance collected into a gummy mass which, when filtered and dried, became hard and granular.

It was found to be extremely soluble in methyl and ethyl alcohol, ether, acetone, chloroform, ethyl acetate and benzene. From solution in all of these liquids it appears as a slightly yellow oil, on evaporation of the solvent at the ordinary temperature. This oil gradually solidifies, requiring sometimes several weeks. From methyl alcohol crystals can be obtained if the solution is kept at 0°. The substance is deposited from ligroin, however, in large, beautiful crystals. They belong to the hemimorphic group of the monoclinic system, for they have a single binary axis of symmetry. The orthopinacoid (100) faces are generally the largest faces on the crystal; the

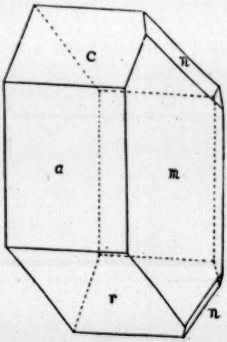


Fig. I.

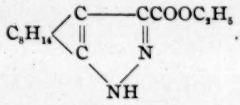
basal pinacoid (001) and the orthodome (101) are also usually well developed. Two small pyramidal faces, opposite each other with respect to the *b* axis, are sometimes, but not always to be found, and the presence of these betrays the hemimorphic character of the crystals. The purified compound melts at 91°–92°. It is insoluble in sodium carbonate solution. Analysis:

I. 0.1620 gram substance gave 0.4001 gram CO_2 and 0.1170 gram H_2O.

II. 0.1867 gram substance gave 19.3 cc. N_2 at 16° and 736 mm.

	Calculated for $C_{14}H_{20}O_3N_2$.	Found.
C	67.74	67.36
H	8.06	8.08
N	11.29	11.50

The composition corresponds to that of ethyl camphylpyrazolecarboxylate,



Hydrolysis, effected by warming for a few minutes with potassium hydroxide solution, yielded camphylpyrazolecarboxylic acid (m. p. 255°–258°), proving the substance to be the one formulated above.

When a portion of the alcoholic hydrochloric acid solution was evaporated to dryness, a solid was obtained which crystallizes readily from acetone in colorless needles, softening at 151° and melting at 156°. An alcoholic solution of this substance yields a precipitate of silver chloride when alcoholic silver nitrate is added. By treatment with a solution of sodium carbonate, ethyl camphylpyrazolecarboxylate is liberated (m. p. 91°–92°). This substance is, therefore, *ethyl camphylpyrazolecarboxylate hydrochloride.* The stability of this salt is noteworthy and unusual.

The Action of Urea and of the Methylated Ureas on Camphoroxalic Acid.

Urea.—Five grams of camphoroxalic acid and 2.7 grams of urea (2 mols.) were dissolved in 50 cc. of 95 per cent alcohol. When the mixture was heated in a bomb, at 100°, for 5 hours, no reaction took place, but when heated in the same manner at 135°, for 5 hours, a compound was formed which melts at 192°–194°, with evolution of gas. It was separated from the crude product of the reaction by evaporating the alcohol on the water-bath, and washing the residue with chloroform.

After being recrystallized twice from methyl alcohol it was in a nearly pure condition, though a slight pink color still clung to it. From its solutions it is deposited in an amorphous form, not in definite crystals.

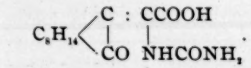
The compound dissolves readily in sodium carbonate solution and is reprecipitated by acidification. Ethyl alcohol dissolves it with ease; acetone, ethyl acetate and chloroform very sparingly; and it is practically insoluble in benzene and ligroin. Analysis:

I. 0.1080 gram substance gave 0.2285 gram CO_2 and 0.0844 gram H_2O.

II. 0.1254 gram substance gave 0.2645 gram CO_2 and 0.0756 gram H_2O.

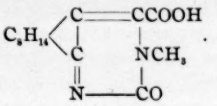
	Calculated for $C_{13}H_{18}O_4N_2$.	Found. I.	II.
C	58.65	57.71	57.53
H	6.77	8.74	6.74

The low results for carbon are due to a slight defect in the absorption apparatus which was not discovered until after the combustions were completed, and time was not available for the preparation of more of the compound. However, the analysis leaves little doubt that the substance is *formamidylcamphoformeneaminecarboxylic acid,*



Methylurea.—Methylurea and camphoroxalic acid, in equimolecular proportions, were heated together in a test-tube, at 95°, for 30 minutes. The temperature was then allowed to rise to 105° for a few minutes. Water and carbon dioxide were eliminated. The cooled mass was crystallized from ethyl acetate by the addition of ligroin, and was then purified by further recrystallization from ethyl acetate. The product is a slightly yellow substance which is deposited in elongated, prismatic, translucent crystals, melting at 154°. Small crystals appear quite colorless. The same compound was obtained when equimolecular proportions of methylurea and camphoroxalic acid, in ethyl alcoholic solution, were heated in a bomb

for 5 hours, at 100°. The substance dissolves very slowly in cold, aqueous sodium carbonate, but with gentle warming it goes into solution readily and is precipitated unchanged on acidification. In cold alcohol it is sparingly soluble, but dissolves readily on heating: in ether, acetone and chloroform it is very soluble, but not quite so easily in benzene, and only slightly so in ligroin. Analysis shows that the ketonic and enolic groups of camphoroxalic acid have reacted, the product being *1-methyl-2-keto-4,5-camphylmetadiazine-6-carboxylic acid,*



Analysis:

I. 0.1967 gram substance gave 0.4612 gram CO_2 and 0.1224 gram H_2O.

II. 0.2227 gram substance gave 21.2 cc. N_2 at 15° and 742 mm.

	Calculated for $C_{14}H_{18}O_3N_2$.	Found. I.	II.
C	64.12	63.95	. .
H	6.87	6.96	. .
N	10.69	. .	10.88

This compound, and also the one from urea, will be investigated more fully at a later date.

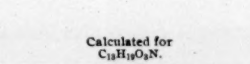
Symmetrical Dimethylurea.—Five grams of camphoroxalic acid (1 mol.) and 4 grams of dimethylurea (2 mols.) were dissolved in 25 cc. of methyl alcohol and heated in a bomb, at 100°–105°, for 5.5 hours. No definite compound could be isolated from the tarry product of the reaction by the use of the ordinary solvents, on account of the extreme solubility of the material. A portion of the mixture, dissolved in alcohol, was poured slowly into sodium carbonate solution, the precipitated tarry matter was filtered out and the clear solution acidified; a small amount of the substance was precipitated which, when dried in the air, melted at 104°–105°. The crude product of the reaction from another experiment, in which the compo-

nents were taken in the same proportion as before, and the conditions of heating were also identical, was worked up as follows: A part of the methyl alcohol was evaporated and the solution poured into aqueous sodium carbonate. The carbonate solution stood over night, and in the morning had the odor of methylamine. After being filtered, it was acidified, and a precipitate appeared of which a part collected in long needles and the remainder in oily drops, that eventually hardened. The substance is extremely soluble in all the ordinary organic media, but can be crystallized from ligroin, separating in long, colorless, prismatic needles which melt at 77°–78°. The substance gives a brownish-red color with alcoholic ferric chloride. Analysis:

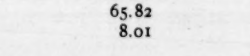
0.1086 gram substance gave 0.2629 gram CO_2 and 0.0787 gram H_2O.

	Calculated for $C_{12}H_{19}O_3N$.	Found.
C	65.82	66.02
H	8.01	8.10

It is apparently, therefore, a methylamine derivative, *methylcamphoformeneaminecarboxylic acid*,



which has not been previously prepared. Its origin is, perhaps, due to a decomposition of the dimethylurea, resulting in the formation of methylamine, which then reacted with camphoroxalic acid; or, what seems more probable, in view of the fact that the odor of methylamine appeared only after the product had stood a long time in sodium carbonate solution, a dimethylurea derivative,



was first formed, having the melting point 104°–105°, and this was hydrolyzed by sodium carbonate into methylamine, car-

bon dioxide and methylcamphoformeneaminecarboxylic acid. Time was not available for pushing these experiments further, but this matter will also be taken up later, in conjunction with the continuation of the study of the action of urea and methylurea on camphoroxalic acid.

Unsymmetrical Dimethylurea.—Camphoroxalic acid and unsymmetrical dimethylurea, in methyl alcoholic solution, were heated in a bomb, first at 100°–105°, then, successively, at 125° and at 140°–145°, in each case for 5 hours. In every experiment the unchanged substances were recovered. After the last heating a very strong odor of dimethylamine was perceptible when the bomb was opened. The experiments were not carried further, as the results gave enough evidence of difference in the action on camphoroxalic acid, of urea and its methyl derivatives to serve our immediate purpose.

The Action of Hydrazine on Camphoroxalic Acid.

A methyl alcoholic solution of hydrazine was prepared by Lobry de Bruyn's method from the hydrochloride, and the strength of the solution approximately determined by means of Fehling's solution. Measured quantities of the solution were then used as desired. For the preparation and titration of the hydrazine solution, we have to thank Mr. W. W. Holland, of this laboratory.

Lobry de Bruyn's directions[1] are not very definite and it may be well, therefore, to state exactly the procedure employed. The quantities given below are convenient and represent suitable proportions of the reacting substances. In a flask fitted with an upright condenser, 100 grams of sodium are added, in small pieces, through the condenser, with the usual precautions, to 150 cc. of absolute methyl alcohol. Forty-two grams (1 mol.) of well pulverized hydrazine hydrochloride are now mixed with the hot mass of sodium methylate (3 mol.). The reaction, which takes place quickly and smoothly, is represented thus:

$$NH_2NH_3Cl + NaOCH_3 = NH_2NH_2 + NaCl + CH_3OH.$$

[1] Rec. Trav. Chim., 13, 433.

After heating a short time, the sodium chloride is filtered out as quickly as possible, with the aid of a suction pump, and the filtrate is distilled from an ordinary fractionating flask. The methyl alcohol which passes off up to about 72° contains only traces of hydrazine. When that temperature is reached the residual, undistilled liquid is placed in a flask to which a Le Bel-Henninge, or similar fractionating apparatus, is attached; it is important to prevent, as far as possible, the hydrazine vapors from coming in contact with the stopper, which should, therefore, be 15–20 cm. above the exit tube. The distillation is then continued under diminished pressure, a manometer being connected with the apparatus. At 30 mm. pressure, the distillate obtained under 50° contained only about 0.5 per cent of hydrazine; between 50° and 60° the fraction contained 2 per cent of the base. The remainder passed over between 60° and 65°, and this solution contained 21 per cent of hydrazine. Throughout the process great care must be taken to avoid unnecessary exposure to the moisture of the air.

Three primary reaction products were obtained by the action of hydrazine on camphoroxalic acid, *viz.*: 1. A compound formed by the action of 1 molecule of hydrazine on 2 of camphoroxalic acid. 2. Hydrazine camphoroxalate. 3. A product resulting from the condensation of 1 molecule of hydrazine with 1 of the acid. The preparation and properties of these substances, in the order mentioned, are described in the succeeding paragraphs.

1. Four grams of camphoroxalic acid were dissolved in the smallest possible amount of methyl alcohol and 3 cc. of a 21 per cent methyl alcoholic solution of hydrazine were added (equimolecular proportions). After standing for 20 hours, the mixture almost completely solidified when it was stirred. The product was recrystallized from methyl alcohol, appearing in the form of long, fine needles which are light yellow in color. It begins to fuse and decompose at about 137°, but complete melting does not take place even at 155°. This crystallized substance was found to contain 2 molecules of methyl alcohol, which are given off slowly at 100°. The compound

obtained by driving off the methyl alcohol is deep yellow in color and decomposes at 150°–155°, without complete fusion. It dissolves readily in aqueous sodium carbonate solution and is reprecipitated on acidification. With alcoholic ferric chloride it gives a slight, brownish-red color, which soon changes to a yellowish green, due to reduction of the ferric to ferrous chloride. It is so extremely soluble in ethyl alcohol, ether, acetone, ethyl acetate, chloroform and benzene that it cannot be crystallized from them, but is left as a sticky mass by the spontaneous evaporation of any one of these solvents. It is soluble in ligroin with difficulty. The crystals with 2 molecules of methyl alcohol are much less soluble than the alcohol-free material. Analysis :

I. 0.3365 gram crystallized substance, when heated at 105°, for 3 hours, lost 0.0395 gram ; for 3 hours longer, 0.0020 gram ; for 2 hours longer, 0.0004 gram. Total loss, 0.0419 gram.

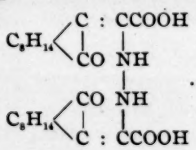
II. 0.2418 gram crystallized substance gave 11.6 cc. N_2 at 11° and 761 mm.

III. 0.1442 gram substance, dried at 100°, gave 0.3432 gram CO_2 and 0.0987 gram H_2O.

	Calculated for $C_{24}H_{32}O_6N_2.2CH_3OH$.	Found. I.	II.
CH_3OH	12.59	12.45	. .
N	5.51	. .	5.73

	Calculated for $C_{24}H_{32}O_6N_2$.	Found.
C	64.86	64.91
H	7.21	7.65

The compound, which may be termed *biscamphoformeneaminecarboxylic acid*, is formed by the action of 1 molecule of hydrazine on 2 molecules of camphoroxalic acid and, presumably, has the formula



2. In another experiment, 4 grams of camphoroxalic acid, in methyl alcoholic solution, were treated with 6 cc. of 21 per cent solution of hydrazine (2 mols.) in methyl alcohol. In a short time a bulky, yellow precipitate appeared which was found to decompose between 160° and 172°. After recrystallization from hot methyl alcohol, it decomposed at 150°–155°, and appeared to be identical with the compound described above. The solubilities of the two substances are markedly different. While the one decomposing at the lower temperature is extremely soluble in all of the ordinary solvents, except ligroin, the new substance is only slightly soluble at the ordinary temperature in methyl and ethyl alcohols, acetone, chloroform, ether, benzene and ligroin. It dissolves on warming, but is changed to the lower melting substance. A solution of sodium carbonate quickly dissolves it, but acidification gives a gelatinous precipitate which is readily soluble in the common organic media, and decomposes at 147°–155°, the change to the other compound having taken place in this process also. This new substance was purified as much as possible by repeated washings with cold alcohol. The purified material is very light yellow in color and begins to decompose at about 186°, complete fusion taking place only at 245°. With alcoholic ferric chloride it gives a slight, brownish-red color, which soon changes to a yellowish-green, due to the production of ferrous chloride. Analysis:

0.1990 gram substance gave 0.4338 gram CO_2 and 0.1375 gram H_2O.

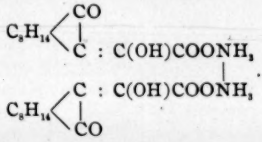
	Calculated for $C_{24}H_{36}O_8N_2$.	Found.
C	60.00	59.45
H	7.50	7.73

The analysis shows that 1 molecule of hydrazine is combined with 2 of camphoroxalic acid:

$$2C_{12}H_{16}O_4 + N_2H_4 = C_{24}H_{36}O_8N_2.$$

On account of its solubility in sodium carbonate solution, it was at first suspected to be formed by the addition of hydrazine to the carbonyl groups, and the change to the other substance

was attributed to the readiness with which water would probably be given off from such an additive compound; it was found, however, that the dried substance, when heated to 160°, for 2 hours, was still unchanged. Further, when a few drops of dilute sulphuric acid were added to a methyl alcoholic solution of the substance, a white, powdery precipitate was formed which was, presumably, hydrazine sulphate. Under similar conditions, the compound decomposing at 150°-155° was not affected, even after standing 20 hours. It appears, therefore, that the compound is *hydrazine camphoroxalate*,



That it is an unstable salt is shown by the fact that sodium carbonate decomposes it in the cold; and also that, when warmed in the presence of solvents, it dissociates, and the hydrazine liberated reacts with the carbonyl groups.

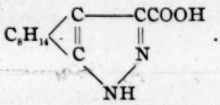
This hydrazine salt was obtained only once. Repeated attempts to prepare it again give only the condensation product.

3. The mother liquors from which the hydrazine salt, or the compound decomposing at 150°-155° was obtained, gave colorless crystals on standing. When recrystallized from acetone, this substance melted at 255°-258°. It was also obtained once as the first product when 2 molecules of hydrazine were added to a methyl alcoholic solution of camphoroxalic acid. The compound was observed to be similar in appearance and in melting-point to the acid, $C_{13}H_{18}O_3N_2$, obtained by the fusion of carbamylcamphoformeneaminecarboxylic acid (Cf. p. 259). Comparison of the two showed them to be identical in all respects and a mixture of them melted at the same temperature as each alone. Analysis:

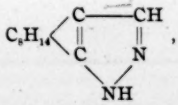
0.1149 gram substance gave 0.2733 gram CO_2 and 0.0793 gram H_2O.

	Calculated for $C_{12}H_{18}O_2N_2$.	Found.
C	65.45	64.87
H	7.27	7.72

As it is formed by the condensation of 1 molecule of camphoroxalic acid with 1 of hydrazine, 2 molecules of water being eliminated, we regard the compound as being camphylpyrazolecarboxylic acid,



In order to obtain, if possible, the simple camphylpyrazole,



some of the acid was subjected to the action of heat. When maintained at 234° for some time, carbon dioxide was evolved copiously and complete fusion eventually took place. The smell of camphor was observed and also a nitrile-like odor. A sublimate of white, prismatic needles, which melted at 217°–218°, with previous softening, appeared in the upper part of the test-tube containing the material. The cooled mass, which was nearly black, was powdered and washed with hot benzene, which removed most of the color. The residue was recrystallized from alcohol and this treatment repeated, but it failed to remove all of the color and analyses of the product did not give concordant results. The substance separates from alcohol in the form of a fine powder, which darkened at about 275°, but was not fused at 288°. It does not dissolve in sodium carbonate solution. When an alcoholic solution of it is reduced with sodium, and nitric acid and potassium bichromate are added, a beautiful, violet color is produced. This indicates a pyrazole. If the compound is camphylpyrazole, its

high melting point is surprising, as phenylcamphylpyrazole melts at 124°–125°.[1]

Biscamphoformeneaminecarboxylic acid, decomposing at 150°–155°, was heated at that temperature for 15 or 20 minutes. There was evolution of carbon dioxide and water vapor, and the smell of camphor was perceptible, together with the nitrile-like odor usually observed in heating these compounds. Complete fusion did not take place, but the whole mass appeared to be affected by the decomposition. The cooled product was powdered and treated with hot benzene. A gelatinous mass remained undissolved, which, after being filtered out and dried, became granular and melted at 222°–223°. The benzene filtrate, when spontaneously evaporated, deposited a gelatinous mass, which was washed with ethyl acetate. The granular solid remaining melted at 232°. The ethyl acetate washings left, on spontaneous evaporation, a red-brown gum in which crystals slowly formed. By washing with small amounts of ethyl acetate these crystals were isolated and then recrystallized from the same solvent. They melted at 221°. When mixed with the above-mentioned substance, melting at 222°–223°, the mixture melted, not sharply, at 215°, some of the latter compound, which was heated simultaneously in a second capillary tube, melting, as usual, at 222°–223°. The two compounds have the same color—a light yellow—but the higher-melting one crystallizes from ethyl acetate in fine needles, which aggregate in nodular clusters, while the low-melting one crystallizes from the same solvent in small, translucent prisms.

The compound melting at 222°–223 is as readily soluble in aqueous sodium carbonate as the substance decomposing at 150°–155°, and is reprecipitated by the addition of acid. It is very soluble in ethyl and methyl alcohols and acetone, but does not readily dissolve in benzene. After two recrystallizations from ethyl acetate, it was analyzed.

I. 0.1308 gram substance gave 0.3127 gram CO_2 and 0.0895 gram H_2O.

II. 0.0905 gram substance gave 0.2172 gram CO_2 and 0.0623 gram H_2O.

[1] Ann. Chem. (Liebig), 281, 353.

III. 0.1319 gram substance gave 7.6 cc. N_2 at 20° and 740 mm.

	Calculated for $C_{24}H_{28}O_4N_2$.	Calculated for $C_{24}H_{30}O_4N_2$.	Found. I.	Found. II.	Found. III.
C	64.86	65.15	65.20	65.45	. .
H	7.21	6.79	7.65	7.70	. .
N	6.30	6.33	. .	. .	6.41

The analyses are scarcely definite enough to enable us to decide with certainty which of the two formulæ belongs to the compound, but the results indicate that it has the composition of the latter. If such be the case, this substance is formed from biscamphoformeneaminecarboxylic acid, $C_{24}H_{32}O_4N_2$, by the loss of 2 atoms of hydrogen.

The substance melting at 232° has a dull yellow color, slightly tinged with red. It readily crystallizes from ethyl acetate. A brick-red deposit usually occurs on the sides of the beaker in which the solution stands; the mother liquors are always red and deposit the same brick-red substance. This colored material appears to be the original substance, mixed with a slight amount of impurity. It melts, not very sharply, at 230°, and mixing with the pure substance raises the melting point close to 232°, the melting point of the pure compound. Recrystallization from ethyl acetate, however, does not remove the color. The compound dissolves very readily in a solution of sodium carbonate, disappearing instantly. Acidification precipitates it unchanged, m. p. 225°–227°. Alcohol, ether and acetone dissolve it with extreme readiness, and in benzene it is moderately soluble, but is very sparingly so in ligroin. The specimen analyzed had been recrystallized twice from ethyl acetate. Analysis:

0.1354 gram substance gave 0.3236 gram CO_2 and 0.0914 gram H_2O.

	Calculated for $C_{24}H_{30}O_4N_2$.	Found.
C	65.15	65.18
H	6.79	7.55

The compound appears, therefore, to be isomeric with that melting at 222°–223°. Further work must be done before

anything can be said with assurance concerning the structure of the two, and even their composition should be tested by additional analyses.

The substance melting at 221° was recrystallized from ethyl acetate and analyzed.

0.0992 gram substance gave 0.2458 gram CO_2 and 0.0662 gram H_2O.

	Calculated for $C_{34}H_{30}O_5N_2$.	Found.
C	67.66	67.58
H	7.04	7.46

The analysis indicates that the compound is an anhydride of biscamphoformeneaminecarboxylic acid.

$$C_{34}H_{32}O_6N_2 \rightarrow C_{34}H_{30}O_5N_2 + H_2O.$$

Various formulas for such a substance are discussed on page 239. It was impossible to make an extended study of this compound on account of the small quantity of material available; indeed the analysis itself should not be accepted without confirmation, on account of the difficulty of determining the degree of purity attained with so small a quantity of the substance. The investigation of these bodies will be continued in this laboratory.

The Action of Phenylhydrazine on Camphoroxalic Acid.

As mentioned on page 240, the following derivatives of phenylhydrazine and camphoroxalic acid had been prepared before this investigation was commenced: 1. Phenylhydrazine camphoroxalate (?). 2. Ethyl camphoroxalate phenylhydrazide, and the corresponding methyl ester. 3. Ethyl and methyl camphylphenylpyrazolecarboxylate. 4. Camphylphenylpyrazolecarboxylic acid, by the hydrolysis of the esters. We have now obtained an addition compound and have prepared the last-named of the above substances (number 4) directly from camphoroxalic acid, but we have failed in our efforts to prepare phenylhydrazine camphoroxalate.

The Addition Compound.—To camphoroxalic acid (1 mol.) in chloroform solution, phenylhydrazine (2 mols.) was added. In a few minutes the mixture suddenly solidified, the substance

formed having a light yellow color and melting at 120°, with decomposition. It was recrystallized from boiling chloroform. The crystals are long and very fine needles, which are somewhat difficult to manipulate on account of their lightness. The compound is easily dissolved by aqueous sodium carbonate, and acidification reprecipitates it. It is readily soluble in alcohol, ether, chloroform and benzene; sparingly soluble in ligroin, and may be recrystallized from hot benzene as well as from chloroform. From these two solvents it sometimes separates as a transparent, gelatinous mass instead of in crystals. With alcoholic ferric chloride a slight brown color is formed; the addition of concentrated nitric acid causes a violent reaction and the production of an intense, reddish-violet color.

The same substance is obtained when phenylhydrazine reacts, at the ordinary temperature, with camphoroxalic acid in alcohol, ether, or benzene solution. It is also formed when the acid (1 mol.), in alcoholic solution, is neutralized with potassium carbonate and treated with phenylhydrazine (1 mol.). Dilution with water and acidification with acetic acid precipitated the yellow compound, melting at 120°. Five grams of camphoroxalic acid and 2.4 grams phenylhydrazine gave 7.4 grams of the substance. Analysis:

I. 0.2367 gram substance gave 0.5602 gram CO_2 and 0.1495 gram H_2O.

II. 0.2559 gram substance gave 0.6043 gram CO_2 and 0.1644 gram H_2O.

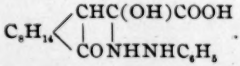
III. 0.1910 gram substance gave 14.7 cc. N_2 at 19° and 747 mm.

IV. 0.1970 gram substance gave 15.6 cc. N_2 at 20° and 746 mm.

	Calculated for $C_{18}H_{24}O_4N_2$.	Found. I.	II.	III.	IV.
C	65.12	64.55	64.41	. .	. .
H	7.28	7.07	7.19	. .	. .
N	8.49	. .	. .	8.69	8.88

The analysis shows that the substance is an addition compound of camphoroxalic acid and phenylhydrazine, and its formation from potassium camphoroxalate excludes the possi-

bility of its being a phenylhydrazine salt of the acid. It must, therefore, be represented by the formula



In the hope of eliminating a molecule of water, some of this compound was placed in a vacuum desiccator containing sulphuric acid, and allowed to stand for 2 months. No change took place. This, and the further fact that its solutions can be boiled, distinguish the substance from the very unstable additive compounds of phenylhydrazine with ketones which have been isolated. This point has been discussed more fully in the theoretical part (*vide* p. 241).

The chloroform mother-liquor, containing the excess of phenylhydrazine from the reaction described above, if allowed to stand a few days at ordinary temperatures, deposited the characteristic, glistening, flaky crystals of phenylhydrazine hydrochloride. The substance was identified by the fact that it gives a precipitate of silver chloride when treated, in alcoholic solution, with silver nitrate; and when aqueous alkali comes in contact with it, phenylhydrazine is liberated.

The purified hydrochloride was found to melt at 233°, with previous darkening, if heated at a slow rate, instead of 240° as given by Broche,[1] or 240°–243° as given by Autenreith.[2] The decomposition of chloroform by phenylhydrazine, with the formation of phenylhydrazine hydrochloride, has been previously noted and investigated by Brunner and his co-workers.[3]

After removal of the phenylhydrazine hydrochloride from the chloroform mother-liquor, it deposited, on standing at the ordinary temperature, a small amount of a substance melting at 196°. When the compound melting at 120° was boiled for 15 or 20 minutes, in alcoholic solution, or when it was heated to fusion without a solvent, the same substance was obtained in relatively large quantity. The latter reaction takes place at 90°–100° if this temperature is maintained for several hours;

[1] J. prakt. Chem., [2], **80**, 114.
[2] Ber. d. chem. Ges., **29**, 1656.
[3] *Ibid.*, **30**, 2587 (1897); **31**, 1406 (1898).

complete fusion occurs, with elimination of water. The substance in question was also formed when camphoroxalic acid was heated with 1, 2 or 3 molecules of phenylhydrazine at 95°–100°, water and a small amount of carbon dioxide being given off in each case. In all these experiments the product was purified by crystallization from alcohol, it being sparingly soluble in cold alcohol and readily in hot. It dissolves very quickly in chloroform, less easily in ether, is readily soluble in benzene and almost insoluble in ligroin. It can be crystallized from benzene as well as from alcohol. Cold, aqueous potassium carbonate dissolves the substance slowly, but on warming a solution is formed quickly, with effervescence. Acidification reprecipitates the substance unchanged.

The crystals deposited from alcoholic solutions were found to have 1 molecule of alcohol of crystallization. Beautiful, colorless crystals were readily obtained which were frequently 5 mm. long and sometimes had a length of 1 cm. They are monoclinic in form, with normal symmetry, *i. e.*, 1 plane and 1 axis of symmetry. The faces observed to be most strongly developed were the basal pinacoid (001), the orthopinacoid

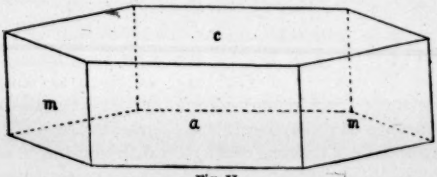


Fig. II.

(100) and the unit prism (110). Orthodome and unit pyramid faces were frequently noticed, but were not well developed. The crystals are flattened parallel to the *b* axis, and present a tubular appearance, as shown in Fig. II. They soon lose their luster, even when kept in closed vessels. The melting-point of the air-dried crystals is not different from that of the substance after expulsion of the alcohol of crystallization. Analysis of the substance dried in a desiccator :

I. 0.2342 gram substance gave 0.5985 gram CO_2 and 0.1606 gram H_2O.

II. 0.2094 gram substance gave 14.2 cc. N_2 at 19° and 765 mm.

III. 0.2190 gram substance gave 14.85 cc. N_2 at 18° and 766 mm.

IV. 0.1468 gram substance, heated in an air-bath for 3 hours, at 125°–135°, lost 0.0179 gram.

	Calculated for $C_{18}H_{20}O_2N_2.C_2H_5OH$.	Found. I.	II.	III.	IV.
C	70.12	69.70	. .	. .	. .
H	7.65	7.67	. .	. .	. .
N	8.20	. .	7.85	7.90	. .
C_2H_5OH	13.45	. .	. .	. .	12.17

Analysis of the substance dried at 125°:

I. 0.2075 gram substance gave 0.5534 gram CO_2 and 0.1302 gram H_2O.

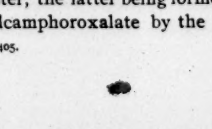
II. 0.1721 gram substance gave 0.4506 gram CO_2 and 0.1085 gram H_2O.

III. 0.2646 gram substance gave 21.8 cc. N_2 at 21° and 755 mm.

IV. 0.2687 gram substance gave 22.7 cc. N_2 at 24° and 748 mm.

	Calculated for $C_{18}H_{20}O_2N_2$.	Found. I.	II.	III.	IV.
C	72.92	72.72	72.86	. .	. .
H	6.80	7.02	7.05	. .	. .
N	9.47	. .	. .	9.32	9.32

The compound is evidently camphylphenylpyrazolecarboxylic acid,



which was previously made by J. Bishop Tingle[1] by hydrolyzing the ethyl ester, the latter being formed from the phenylhydrazide of ethylcamphoroxalate by the action of heat, by

[1] THIS JOURNAL, 19, 405.

the dehydrating action of hot glacial acetic acid, or of hydrochloric acid, in alcoholic solution. He found that the substance crystallizes from benzene with 0.5 molecule of benzene of crystallization. He also mentions that the acid gives no color with concentrated nitric acid, while the ester gives a pale yellow color. We find that if the solution of the acid, in concentrated nitric acid, is very gently warmed, this pale yellow color appears. An alcoholic solution of ferric chloride gives, with the acid, a red color bordering on orange.

An attempt to make camphylphenylpyrazole carboxylic acid by condensing phenylhydrazine and camphoroxalic acid, in benzene solution, in the presence of fused calcium chloride, did not proceed satisfactorily. The addition compound, melting at 120°, was first formed. The products of the reaction were boiled on a water-bath, in a flask with a return condenser, until this addition compound disappeared, which required several hours. Considerable quantities of phenylhydrazine hydrochloride separated out, the hydrochloric acid doubtless being liberated by the formation of calcium salts of camphoroxalic acid and the acids derived from it by the action of phenylhydrazine. The benzene filtrate from the hydrochloride and the calcium chloride was evaporated to dryness, the residual mass dissolved in alcohol, and the solution poured into a solution of potassium carbonate. Dilution with water and acidification precipitated a small amount of camphylphenylpyrazolecarboxylic acid. No other products of the reaction were found.

J. Bishop Tingle[1] has described a compound, melting at 214°–215° with previous darkening, which he obtained when camphoroxalic acid and 2 molecules of phenylhydrazine, in anhydrous ethereal solution, were boiled for 2 hours in an apparatus with a return condenser. This compound was supposed to be phenylhydrazine camphoroxalate, but was not analyzed. Attempts were made to obtain the substance again for further study, but when the ethereal solutions of camphoroxalic acid and phenylhydrazine were poured together, the additiom com-

[1] THIS JOURNAL, **20**, 328 (1898).

pound, m. p. 120°, was at once formed, the whole mass solidifying and the ether boiling with the heat of the reaction.

Boiling on the water-bath, with a return condenser, for 3 hours, produced no change in the mass, even when more ether was added. The experiment was repeated, both with ordinary ether and with ether dried over sodium, with the same result. Attempts to get the phenylhydrazine salt of camphylphenylpyrazolecarboxylic acid, by treating the acid with excess of phenylhydrazine, were likewise unavailing.

The Action of Parabromphenylhydrazine on Camphoroxalic Acid.

The compounds obtained by the action of parabromphenylhydrazine on camphoroxalic acid correspond fully to those obtained with phenylhydrazine, with the exception of one substance, which has the composition of the addition compound minus 1 molecule of water. Such a body was not obtained in the phenylhydrazine series.

Two compounds, which melt at 149° and 172°, respectively, are formed whenever camphoroxalic acid and parabromphenylhydrazine are brought together in alcoholic solution. What experimental factors determine which shall be produced in larger quantity were not learned. Under seemingly similar conditions, sometimes one and sometimes the other separates first, and in one experiment the two separated at the same time, each in its characteristic crystalline form. When crystals of one substance have been separated and completely removed from the solution, the mother-liquor usually next deposits crystals of the other compound. The length of heating is not the determining factor, for either may be obtained without any heating at all. Although the substance melting at 172° was first obtained by evaporating the solution to a small volume and allowing it to stand, the other compound separated first in another experiment in which the substances, in absolute alcoholic solution, were boiled in a flask with a return condenser for an hour and a half, the solution being evaporated to a small volume and allowed to stand. It is possible that the concentration of the parabromphenylhydrazine may determine the relative amounts of the two compounds, because it was

observed that with a small volume of solvent, and a large excess of this substance, more of the low-melting, additive compound was obtained. The method of procedure given in the succeeding detailed description of the experiments is the one employed when these two substances were obtained for the first time. Repetition of the experiments may or may not give the same results.

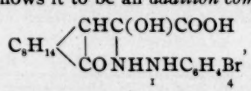
Two and one-half grams of camphoroxalic acid (1 mol.) and 4 grams parabromphenylhydrazine were dissolved in a small amount of alcohol and the solution warmed for a few minutes. The reaction mixture then solidified rather suddenly into a yellow mass. The substance was filtered and recrystallized from alcohol. It forms very slender, yellow needles, which melt at 149° with evolution of gas. The compound is readily soluble in methyl and ethyl alcohols, extremely soluble in acetone and chloroform, fairly so in ether and benzene, but is soluble with difficulty in ligroin. From alcohol or benzene solution it sometimes separates out as a transparent, gelatinous mass. It dissolves readily in aqueous sodium carbonate and is reprecipitated by acidification. With ferric chloride, in alcoholic solution, only a slight brownish color is produced. Concentrated nitric acid attacks it violently, with the formation of a deep red color. Analysis:

I. 0.2409 gram substance gave 0.4603 gram CO_2 and 0.1150 gram H_2O.

II. 0.1801 gram substance gave 0.0786 gram AgBr.

	Calculated for $C_{18}H_{23}O_4N_2Br$.	Found. I.	II.
C	52.53	52.14	. .
H	5.63	5.34	. .
Br	19.46	. .	18.57

The analysis shows it to be an *addition compound*,



corresponding to that formed with phenylhydrazine, m. p. 120°, which it resembles in appearance and behavior. In order to test its stability, it was boiled for 2 hours with abso-

lute alcohol, but it remained unchanged. The same point was further proved by the fact that the compound, when warmed with acetic anhydride to about 75°, for an hour, was precipitated unchanged on dilution with water. Such behavior, as pointed out in the earlier portion of this paper, is a strong argument against the substance being a ketone additive compound, of the usual type ascribed to such substances.

Carbon and hydrogen in this compound, and in the others containing bromine which are described subsequently, were determined in the presence of copper oxide, by the method recently worked out by one of us.[1]

Seven and one-half grams of camphoroxalic acid and 6.5 grams (1 mol.) of parabromphenylhydrazine were dissolved in alcohol and boiled on the water-bath to a small volume. On standing over night, crystals were deposited which melt at 172°, with evolution of gas. The substance may be recrystallized readily from alcohol. Very perfect, though not large, crystals are formed which belong to the orthorhombic system. The macrodome (101) and brachydome (011) forms are strongly developed, and the crystals frequently approach the octohedron in shape, but are usually elongated somewhat in the *c* axis. The macropinacoid form (100) is often present as a small face. The crystals are not colorless even after repeated crystallizations, but have a slight brownish tinge. In recrystallizing the substance, crystals of a different kind were sometimes deposited in very small amount. These were light-yellow colored needles, aggregated in fan-like clusters, and were not lustrous like the other variety. They melted at the same temperature, 172°, as the orthorhombic crystals, but were obtained in too small amount for further comparison. The substance is very soluble in ether, acetone and chloroform; readily in methyl and ethyl alcohols; sparingly in benzene; and soluble with difficulty in ligroin. It does not dissolve in aqueous sodium carbonate, even on boiling, and warm alkali hydroxide solution does not dissolve it, but slowly effects hy-

[1] C. J. Robinson: THIS JOURNAL, 36, 531 (1906).

drolysis. It is soluble in alcoholic alkali hydroxide, but rapid decomposition takes place, with the formation of a red color, probably due to free parabromphenylhydrazine. However, if an alcoholic solution of the compound is poured into a solution of sodium carbonate it is not precipitated by the addition of water, but comes down unchanged, m. p. 169°, on acidification. Its extreme insolubility in water presumably prevents its going into solution in aqueous alkali.

An alcoholic solution of ferric chloride gives, with this substance, a peculiar, dull brownish-red color, and the addition of water causes a blue fluorescence. Analysis:

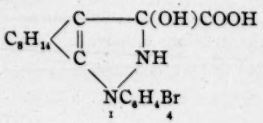
I. 0.2135 gram substance gave 0.4308 gram CO_2 and 0.0982 gram H_2O.

II. 0.2624 gram substance gave 16.2 cc. N_2 at 19° and 758 mm.

	Calculated for $C_{18}H_{11}O_2N_2Br$.	Found. I.	II.
C	54.94	55.03	. .
H	5.38	5.15	. .
N	7.14	. .	7.08

The crystallized substance did not change in weight when heated at 110°, for 2 hours.

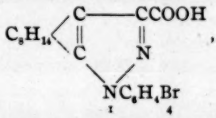
This compound has the same composition as the addition product, melting at 149°, minus 1 molecule of water. The latter is attacked by concentrated nitric acid with almost explosive violence, while the present substance, when treated with the same reagent, goes into solution slowly and quietly, and a pale yellow color is developed. In this respect, as well as in its crystallizing power, it is analogous to camphylphenylpyrazolecarboxylic acid. Hence it seems probable that the compound melting at 172° contains the pyrazole ring, although only 1 molecule of water has been eliminated. As stated in the theoretical part,



seems the preferable one of the three formulæ possible for such a substance.

An attempt was made to acetylate the compound melting at 172° by the action of acetic anhydride. When heated with the anhydride alone, the substance did not dissolve, but on the addition of a few drops of concentrated sulphuric acid, solution took place at once, however, only a tarry mass was formed from which no definite product could be isolated.

Camphylparabromphenylpyrazolecarboxylic acid,



was obtained by the action of heat on either of the two compounds described above. A quantity of the addition compound, which had not been completely purified, was placed in a test-tube and heated in a sulphuric-acid bath, the temperature being raised slowly. At 110° it began to give off water, and partial fusion took place, but eventually the entire mass became solid again and further heating to 135° gave no action except the elimination of a small quantity of carbon dioxide. The cooled mass was brown and brittle. It was powdered and dissolved in boiling benzene. On cooling, a colorless substance was deposited which melts at 215° when heated slowly. The procedure with the compound melting at 172° was similar. It began to decompose after heating for some time at 155°, and partial fusion took place, with the elimination of water. After a few minutes the material again became solid. The cooled mass was treated in the same way as in the case of the addition compound, and the two products were found to be identical.

This new compound dissolves slowly in cold sodium carbonate solution, but readily when warmed. Acidification reprecipitates it. It crystallizes from benzene or alcohol in clusters of small needles, the clusters often being nodular in appearance. It is readily soluble in ether, acetone, chloroform and ethyl acetate, but is almost insoluble in ligroin. Analysis:

0.1937 gram substance gave 0.4095 gram CO_2 and 0.0923 gram H_2O.

	Calculated for $C_{18}H_{19}O_2N_2Br$.	Found.
C	57.58	57.66
H	5.10	5.33

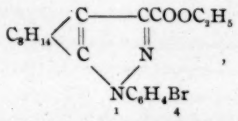
The analysis shows it to be *camphylparabromphenylpyrazolecarboxylic acid*, with the formula given above.

Ethyl camphylparabromphenylpyrazolecarboxylate was obtained by the action of absolute alcohol and hydrochloric acid on the addition compound, m. p. 149°. The latter substance was dissolved in absolute alcohol, and the solution saturated with dry hydrochloric acid gas, the liquid being cooled with ice-water. After standing 2 days, the mixture was poured into water. A slightly yellow substance was precipitated which was filtered, dried and found to melt at 105°. No further precipitate was produced by neutralizing the filtrate with sodium carbonate. To remove any acid that might be present in the precipitated substance it was dissolved in alcohol, the solution was treated with dry sodium carbonate and allowed to stand for several hours. The liquid was then filtered, and the filtrate poured into water. An emulsion was formed which, after the addition of sodium chloride, was extracted with ether. Evaporation of the ether left an oily substance which was readily crystallized from acetone, and purified by recrystallization from the same solvent. Magnificent crystals were formed, which always appeared somewhat yellow, though translucent, but were colorless when powdered. Some of the crystals were nearly 1 cm. in length. They belong to the triclinic system and, apparently, to the asymmetric group of that system. The pure compound melts at 107°. It does not dissolve in sodium carbonate, and gives no color with ferric chloride. It is extremely soluble in chloroform and benzene, very soluble in ether and acetone, readily in alcohol, and slightly in ligroin. Dilute sulphuric acid does not dissolve it, even in 50 per cent alcoholic solution. Analysis:

0.2125 gram substance gave 0.4624 gram CO_2 and 0.1045 gram H_2O.

	Calculated for $C_{20}H_{23}O_2N_2Br$.	Found.
C	59·52	59·35
H	5·75	5·50

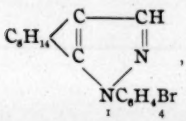
The substance is, therefore, *ethyl camphylparabromphenylpyrazolecarboxylate*,



which is formed from the addition compound by a condensation involving the loss of two molecules of water, and the formation of a pyrazole ring, esterification taking place also. The fact that it does not dissolve in acid shows that it is only very slightly basic, if at all. In contrast with this compound, ethyl camphylpyrazolecarboxylate forms a stable salt with hydrochloric acid (Cf. p. 233).

An attempt to prepare camphylpyrazolecarboxylic acid from camphylparabromphenylpyrazolecarboxylic acid, by oxidizing away the bromphenyl group, was not successful. The experiment was carried out with potassium permanganate, in boiling acetone solution, but the original substance was recovered unchanged.

What appears to be *camphylparabromphenylpyrazole* was obtained from the carboxylic acid by the action of heat. The acid fuses at 215°, and it was maintained at 215°–218° until evolution of carbon dioxide ceased, which required about an hour for 3·5 grams. The cooled mass was vitreous, very lustrous and appeared black, but in small pieces it was only slightly brown, and was nearly transparent. It was found to be extremely soluble in all the ordinary organic solvents, including ligroin, and was left as an oily residue on spontaneous evaporation. On this account, we were unable to purify the small quantity of the substance which we had at our disposal and, therefore, no analysis was obtained. It is, without much doubt, camphylparabromphenylpyrazole,



because the analogous compound, camphylphenylpyrazole, is described by Bishop, Claisen and Sinclair[1] as having similar properties, and being very difficult to crystallize.

The Hydration Product of Camphoroxalic Acid.

Some years ago, Bishop Tingle[2] found that when camphoroxalic acid is heated with dilute, aqueous hydrochloric or sulphuric acid, a product is formed which gives an intense blue color with alcoholic ferric chloride solution, and has the composition of camphoroxalic acid plus 2 molecules of water. A further investigation of this substance was undertaken to determine, if possible, its structure, but on account of the extreme instability of the compound, the study has not yet been carried very far, but will, it is hoped, be taken up at a future date.

The substance was prepared as described by Bishop Tingle, by heating 6 grams of camphoroxalic acid with 25 cc. of 1 : 3 sulphuric acid, in a closed tube, at 135°–140°, for 9 to 10 hours. Variations in the concentration of the acid and in the temperature showed that the best results were obtained under the conditions described. The product had the horny appearance mentioned in the previous work, but crystals were observed only when the tubes were well filled, and the pressure, consequently, high. The yield was also improved by a high pressure. It appears to be best to fill the tubes nearly two-thirds full. The product has an aromatic odor, suggestive of fresh pine. It was purified by extracting in a Soxhlet apparatus with low-boiling ligroin, until the substance remaining in the extraction apparatus gives a pure blue color with alcoholic ferric chloride solution; this substance is then recrystallized from chloroform by the addition of ligroin. Temperatures above 60° must be avoided, as the compound reverts with the utmost readiness to camphoroxalic acid, therefore, the ligroin used for this extraction should

[1] Ann. Chem. (Liebig), **281**, 353.
[2] This Journal, **20**, 329 (1898).

boil below 60°, and solutions of the substance should not be warmed. It crystallizes with difficulty in nodular forms, which melt at 92°. The color reaction with ferric chloride is not instantaneous; first a yellow color appears, which changes gradually, through green, to a rich blue. Addition of water to the colored, alcoholic solution converts it to a bluish-violet. Analysis of the substance gave results agreeing with those obtained by Bishop Tingle.

The acid liquid from the tubes in which the reaction takes place contains some of the product, which can be recovered by extraction with ether. This liquid, before extraction with ether, has a strong odor like that of pine, as described above. When warmed, it gives up a small amount of carbon dioxide.

The hydration product yielded no salt when treated with barium chloride, but with barium hydroxide a salt was obtained which is readily soluble in water, fairly soluble in 50 per cent alcohol, but insoluble in absolute alcohol even on boiling. It was not analyzed. When the hydrated acid was treated carefully with aqueous sodium carbonate, of known strength, till litmus paper showed neutrality, 4 equivalents of the carbonate were required, indicating the tetrabascity of the acid. This was only an approximate determination.

When dissolved in chloroform, in the presence of 2 mols. of aniline, the substance yields, at the ordinary temperature, a compound melting at 158°, which is, apparently, identical with the product obtained under similar circumstances with camphoroxalic acid. The sodium salt, in aqueous solution, at room temperature, yields a compound with semicarbazine which melts at 200° and is identical with the substance obtained with camphoroxalic acid.

To an aqueous solution of the sodium salt there was added a solution of 2 molecules of hydroxylamine, obtained from the hydrochloride by the use of sodium carbonate; the mixture was allowed to remain for several days without heating. A colorless product is formed which is not precipitated by acidification, but can be extracted with ether. It melts, with decomposition, at 181°–182°. No product of hydroxylamine

with camphoroxalic acid is known which has such a melting point. On account of the difficulty of preparing pure material in quantity, these investigations were not carried further.

JOHNS HOPKINS UNIVERSITY,
May, 1906.

Contributions from the Sheffield Laboratory of Yale University.

CXXXIV. — RESEARCHES ON FURFURANS: ON 2,5-DICARBETHOXY-3,4-DIKETOTETRAHYDROFURFURAN. I.

BY TREAT B. JOHNSON AND CARL O. JOHNS.

In a recent publication from this laboratory, Johnson and McCollum[1] have shown that ethyl formate condenses with diethyl glycollate, I., in the presence of metallic sodium, to form the sodium salt of ethyl α-ethoxy-β-hydroxyacylate, II. :

$$\underset{\text{I.}}{C_2H_5OCH_2COOC_2H_5} + HCOOC_2H_5 + Na = \underset{\text{II.}}{NaO\overset{\ominus}{C}H : C(OC_2H_5)COOC_2H_5} + C_2H_5OH.$$

It has also been observed by Wislicenus[2] that diethyl oxalate can condense with 2 molecular proportions of ethyl acetate, in the presence of sodium ethylate, to form the disodium salt of diethyl ketipate, III. :

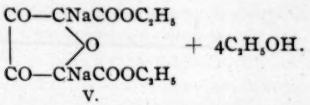
$$C_2H_5OCOCOOC_2H_5 + 2CH_3COOC_2H_5 + 2C_2H_5ONa = \underset{\text{III.}}{C_2H_5OCOCHNaCOCOCHNaCOOC_2H_5} + 4C_2H_5OH.$$

It seemed probable to the writers that diethyl oxalate might condense with diethyl diglycollate, IV., to form the disodium salt of 2,5-dicarbethoxy-3,4-diketotetrahydrofurfuran, V. We find that this condensation takes place in the normal manner, according to the following equation :

$$C_2H_5OCOCOOC_2H_5 + \underset{\text{IV.}}{C_2H_5OCOCH_2OCH_2COOC_2H_5} + 2C_2H_5ONa =$$

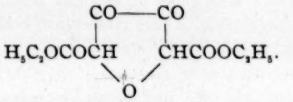
[1] J. Biol. Chem., 1, 437.

[2] Ber. d. chem. Ges., 20, 591. Ann. Chem. (Liebig), 246, 328.



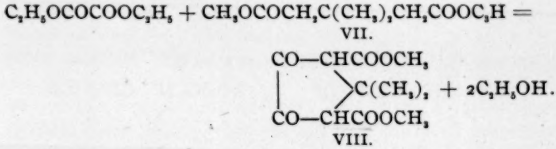
V.

When this salt, V., was treated with acids a crystalline ester, VI., was obtained.



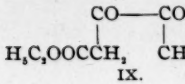
VI.

This condensation is analogous to that described by Komppa.[1] He found that diethyl oxalate condensed with dimethyl β,β-dimethylglutarate, VII., to give the dimethyl diketoapocamphorate, VIII. :

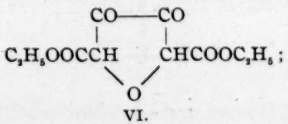


VII. VIII.

The relationship between diethyl ketipate, IX., 2,5-dicarbethoxy-3,4-diketotetrahydrofurfuran, VI., and dimethyl diketoapocamphorate, VIII., is illustrated by the following formulas :

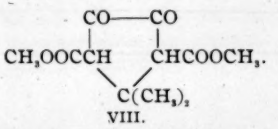


IX.



VI.

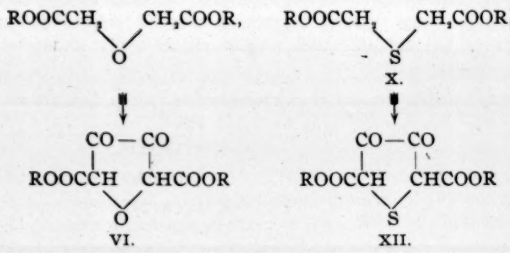
[1] Ber. d. chem. Ges., **32**, 1421 ; **34**, 2472 ; **36**, 4332. Dieckmann : *Ibid.*, **32**, 1933.



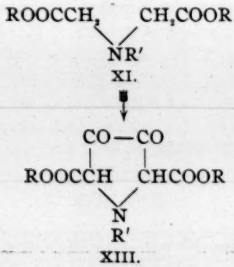
VIII.

2,5-Dicarbethoxy-3,4-diketotetrahydrofurfuran, VI., is a representative of a new class of ketonic tetrahydrofurfurans. The study of derivatives of this interesting body is in progress in this laboratory.

We shall also attempt to condense diethyl oxalate with esters of thiodiglycollic acid, X., and nitrogen substituted iminodiacetic acids, XI.



VI. XII.



XI. XIII.

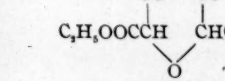
2,5-Dicarbethoxy-3,4-diketotetrahydrothiophene, XII., would be a representative of the unknown series of tetrahydro-

thiophanes. The term "thiophane" is ascribed by Mabery[1] to this new class of compounds. This series is of interest since Mabery's[2] investigations seem to indicate that tetrahydrothiophenes are present in the sulphur oils of Canadian petroleum.

EXPERIMENTAL.

The diglycollic acid that was used in this work was prepared according to directions given by Lossen.[3]

2,5-Dicarbethoxy-3,4-diketotetrahydrofurfuran,



$C_2H_5OOCCH \quad CHCOOC_2H_5$.—This derivative was prepared in the following manner: The calculated quantity of sodium ethylate was obtained by digesting 4 grams of metallic sodium and 8 grams of absolute alcohol in ether, until the sodium disappeared. A mixture of 11.5 grams of diethyl oxalate and 15 grams of diethyl diglycollate were then slowly added to the ether solution. There was an immediate reaction and sufficient heat was evolved to cause the ether to boil. A yellow sodium salt deposited on cooling. The mixture was allowed to stand about 5 days, when the salt was filtered off and dried in the air. The yield of salt was practically quantitative. When an aqueous solution of this salt was acidified with dilute sulphuric acid a colorless, crystalline deposit was obtained. The compound was very soluble in hot alcohol. It deposited, on cooling, in stout, prismatic crystals that melted at 189°, without effervescence, to a clear oil. Analysis:

0.2900 gram substance gave 0.5207 gram CO_2 and 0.1387 gram H_2O.

	Calculated for $C_{10}H_{12}O_7$.	Found.
C	49.18	48.97
H	4.92	5.3

[1] THIS JOURNAL, **35**, 404.
[2] *Loc. cit.*
[3] Ann. Chem. (Liebig), **343**, 121 (1905).

Sodium Salt of 2,5-Dicarbethoxy-3,4-diketotetrahydrofurfuran.—This salt was prepared for analysis by dissolving 1 gram of the furfuran derivative in alcohol containing 2 molecular proportions of sodium ethylate. The salt deposited as a white, microscopic powder. A sodium determination gave the following result:

0.1012 gram salt gave 0.0512 gram Na_2SO_4.

	Calculated for $C_{10}H_{10}O_7Na_2$.	Found.
Na	15.97	16.3

NEW HAVEN, CONN.,
June 5, 1906.

Contributions from the Sheffield Laboratory of Yale University.

CXXXV.—ORTHO-, META- AND PARAIODHIPPURIC ACIDS.

BY TREAT B. JOHNSON AND HAROLD A. MEADE.

The object of the work described in this paper was to synthesize ortho-, meta- and paraiodhippuric acids. We shall also describe some new derivatives of 3,5-dinitrobenzoic acid.

Our interest in iodhippuric acids was incited by a recent paper—"Ueber den physiologischen Abbau von Iodalbumin"—by Mosse and Neuberg,[1] in which the authors have described some interesting end products of the metabolism of iodine-albumin[2] when fed to dogs and rabbits. They isolated from the blood of dogs an iodine derivative that was identified as orthoiodbenzoic acid, "the melting point of which corresponded to that given for the ortho acid, 156°–157°, by Kekulé.[3] Wachter[4] has shown that this acid melts at 162°." From the urine of rabbits they separated the barium salt of a new, iodine substituted acid. Their analytical determinations agreed with the calculated values for a salt of iodhippuric acid. This acid was not obtained in a pure condition. They concluded, nevertheless, that they were dealing with an ortho de-

[1] Z. physiol. Chem., **37**, 427 (1903).

[2] "Zu die Untersuchungen, diente ein technisches Product, das lösliche Iodeigonnatrium von der chemischen Fabrik Helfenberg in Sachsen (Mosse and Neuberg)."

[3] Ber. d. chem. Ges., **7**, 1007 (1874).

[4] *Ibid.*, **26**, 1744 (1893).

rivative because it was converted into glycocoll and orthoiodbenzoic acid[1] when heated with hydrochloric acid.

Our knowledge of iodine substituted hippuric acids is very limited. Only 2 iodhippuric acids are mentioned in "Beilstein's Handbuch."[2] One was prepared by J. Maier[3] by warming hippuric acid with an alcoholic solution of iodine. While the structure of this acid is not known, it probably is to be represented by one of the two following formulas :

$$\underset{\text{I.}}{C_6H_5CONHCHICOOH} \quad \text{or} \quad \underset{\text{II.}}{C_6H_5CONICH_2COOH}.$$

It is not identical with any one of the 3 iodhippuric acids that we describe in this paper.

The second iodhippuric acid mentioned was synthesized by Griess.[4] It was prepared by treating diazohippuric acid with hydriodic acid, and is represented in the literature as a meta derivative. Griess does not state in his paper how he obtained his diazohippuric acid, but it is assumed that he synthesized it from metanitrohippuric acid, which was prepared by the nitration[5] of hippuric acid.

We prepared ortho and paraiodhippuric acids by treating glycocoll, in alkaline solution, with orthoiodbenzoyl chloride,[6] III., and paraiodbenzoyl chloride,[7] IV., respectively.

$$NH_2CH_2COOH + \underset{\text{III.}}{{}^{2}IC_6H_4{}^{1}COCl} \rightarrow \underset{\text{(m. p. 167°.) V.}}{{}^{2}IC_6H_4{}^{1}CONHCH_2COOH};$$

$$\underset{\text{IV.}}{{}^{4}IC_6H_4{}^{1}COCl} \rightarrow \underset{\text{(m. p. 193°.) VI.}}{{}^{4}IC_6H_4{}^{1}CONHCH_2COOH}.$$

The ortho acid melted at 167° and the para at 193°. Orthoiodhippuric acid possesses the peculiar property of depositing from hot water as an oil, which crystallized on standing.

[1] *Loc. cit.*
[2] Vol. II., 1187.
[3] Z. f. Chem., 1865, p. 415. Am. J. Sci., [2], **39**, 209.
[4] Ber. d. chem. Ges., **1**, 190 (1868).
[5] Schwanert : Ann. Chem. (Liebig), **112**, 69. Conrad : J. prakt. Chem., [2], **15**, 254.
[6] Wachter : *Loc. cit.*
[7] Hoffmann : Ann. Chem. (Liebig), **264**, 167.

When the acid was impure we had much difficulty in getting it to assume a crystalline form. This behavior suggests why Mosse and Neuberg obtained their iodhippuric acid as a syrup.[1]

Metaiodhippuric acid was obtained in the following manner: Metanitrohippuric acid, VIII., was prepared from glycocoll and metanitrobenzoyl chloride, VII., according to the equation:

$$NH_2CH_2COOH + \underset{\text{VII.}}{\overset{3}{N}O_2C_6H_4\overset{1}{C}OCl} + NaOH = \underset{\text{VIII.}}{\overset{3}{N}O_2C_6H_4\overset{1}{C}ONHCH_2COOH} + H_2O + NaCl.$$

The nitro acid was then reduced to aminohippuric acid with ammonium sulphide.[2] When the amino acid was diazotized and warmed with potassium iodide, it was converted into metaiodhippuric acid. Griess gave no melting point for his acid. Our acid melted at 156°. It agreed in its crystalline form and solubility with the iodine acid described by Griess.

EXPERIMENTAL.

o-Iodhippuric Acid,

.—This iodhippuric acid was obtained in the form of its sodium salt by treating an aqueous solution of 1.3 grams of aminoacetic acid and 1.4 grams of sodium hydroxide with 3.8 grams of orthoiodbenzoyl chloride (Schotten-Baumann reaction). When the alkaline solution was acidified with hydrochloric acid the iodhippuric acid deposited as a colorless, crystalline solid. It was purified for analysis by recrystallization from hot water. It deposited, on cooling, as an oil, that finally crystallized in clusters of radiating needles. They melted at 167°, without effervescence, to a clear oil. Analysis (Kjeldahl):

[1] "— resultiert eine Lösung der freien Säure, die sich beim Eindampfen als Syrup an den Gefässwandungen abscheidet."

[2] Schwanert: Ann. Chem. (Liebig), 112, 70.

	Calculated for $C_9H_9O_3NI$.	Found. I.	II.
N	4.59	4.48	4.50

The orthoiodbenzoic acid and orthoiodbenzoyl chloride that were used in the above experiment were prepared according to the directions of Wachter.[1]

o-Iodbenzoylaminoacetonitrile, $IC_6H_4CONHCH_2CN$.—A solution of aminoacetonitrile was prepared by dissolving 20 grams of the aminoacetonitrile sulphate[2] and 10 grams of sodium hydroxide in cold water. The calculated quantity of orthoiodbenzoyl chloride was then added to this solution, in small portions and the mixture thoroughly shaken. The nitrile separated as a colorless solid. The yield was practically quantitative. It deposited from alcohol in prisms, which melted, at 158°, to a clear oil. Analysis (Kjeldahl) :

	Calculated for $C_9H_7ON_2I$.	Found.
N	9.80	10.00

Ethyl o-Iodhippurate, $IC_6H_4CONHCH_2COOC_2H_5$.—Dry hydrochloric acid gas was passed into a hot, alcoholic solution of the above nitrile for 3 hours. The solution was then evaporated to dryness. We obtained a crystalline residue that was washed with cold water to remove ammonium chloride. The ester was extremely soluble in alcohol and benzene. It was purified for analysis by crystallizing from a mixture of ligroin and benzene. It separated as an oil and finally crystallized in the form of irregular prisms, which showed signs of melting at 70°, and then melted, at 79°–80°, to a clear oil. Analysis (Kjeldahl) :

	Calculated for $C_{11}H_{13}O_3NI$.	Found.
N	4.20	4.34

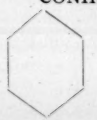
[1] Ber. d. chem. Ges., **36**, 1744.
[2] Klages: *Ibid.*, **36**, 1511.

m-Iodhippuric Acid, .—This acid was

prepared by warming an aqueous solution of potassium iodide and metadiazohippuric acid.[1] It deposited from hot water in scales or thin plates that melted at 155°–156°. Analysis (Kjeldahl):

	Calculated for $C_9H_9O_3NI$.	Found.
N	4·59	4·9

The metaaminohippuric acid required for this preparation was obtained in the following manner: Metanitrobenzoic acid was first made according to the method described by Hübner,[2] and then converted into the chloride with phosphorus pentachloride.[3] Metanitrohippuric acid was prepared by treating aminoacetic acid with metanitrobenzoyl chloride, according to Schotten-Baumann's reaction and the nitro acid was reduced to aminohippuric with ammonium sulphide.

p-Iodhippuric Acid,  .—When amino-

acetic acid was treated with paraiodbenzoyl chloride, under the same conditions as used in the preparation of orthoiodhippuric acid, it was converted, quantitatively, into this acid. It was difficultly soluble in cold water, but deposited from hot water in plates that melted at 193°. Analysis (Kjeldahl):

	Calculated for $C_9H_9O_3NI$.	Found.
N	4·59	4·55

[1] Griess: Ber. d. chem. Ges., 1, 490.
[2] Ann. Chem. (Liebig), 222, 72.
[3] Claisen and Thompson: Ber. d. chem. Ges., 12, 1943.

The paraiodbenzoic acid required for this experiment was prepared according to the method described by Körner,[1] by oxidizing paraiodtoluene with potassium bichromate and sulphuric acid.

p-Iodbenzoylaminoacetonitrile, $^{4}IC_6H_4{}^{1}CONHCH_2CN$, obtained from paraiodbenzoyl chloride and aminoacetonitrile, in presence of excess of sodium hydroxide, was purified for analysis by recrystallization from alcohol. It deposited in prismatic crystals that melted at 191°–192°. Analysis (Kjeldahl):

	Calculated for $C_9H_7ON_2I$.	Found.
N	9.80	9.55

Di-p-iodbenzoylaminoacetonitrile, $(^{4}IC_6H_4{}^{1}CO)_2NCH_2CN$.—This was obtained as the chief product of the reaction in one experiment when we proceeded as follows: Three grams of aminoacetonitrile sulphate and 3 molecular proportions of sodium hydroxide were dissolved in water. When this solution was shaken with 5 grams of paraiodbenzoyl chloride the nitrile deposited as a white, crystalline solid. It crystallized from alcohol in clusters of radiating prisms that melted at 215°–216°. Analysis (Kjeldahl):

	Calculated for		Found.	
	$C_{18}H_{10}O_2N_2I_2$.	$C_9H_7ON_2I$.	I.	II.
N	5.42	9.80	5.49	5.59

Ethyl p-iodhippurate, $^{4}IC_6H_4{}^{1}CONHCH_2COOC_2H_5$, was prepared by saturating an alcoholic solution of the above nitrile with hydrochloric acid gas and then warming for a few hours on the steam-bath. It was purified for analysis by recrystallization from alcohol and deposited in plates that melted, at 128°–129°, to a clear oil. Analysis (Kjeldahl):

	Calculated for $C_{11}H_{13}O_3NI$.	Found.
N	4.20	4.44

p-Iodbenzoylanilide, $^{4}IC_6H_4{}^{1}CONHC_6H_5$, prepared from aniline and paraiodbenzoyl chloride, was purified for analysis by recrys-

[1] Zeit. f. Chem., 1868, p. 327.

tallization from 95 per cent alcohol. It melted at 210°, without effervescence. Analysis (Kjeldahl):

	Calculated for $C_{13}H_{10}ONI$.	Found.
N	4.33	4.52

3,5-Dinitrobenzoylanilide, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ONHC_6H_5$, from 3,5-dinitrobenzoyl chloride[1] and aniline, crystallized from alcohol in needle-like prisms, that melted at 234°–235°. Analysis (Kjeldahl):

	Calculated for $C_{13}H_9O_5N_3$.	Found.
N	14.63	14.46

3,5-Dinitrobenzoylparatoluidide, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ONHC_6H_4\overset{1}{C}H_3$.—This compound was practically insoluble in water and the ordinary organic solvents. It did not melt below 280°. Analysis (Kjeldahl):

	Calculated for $C_{14}H_{11}O_5N_3$.	Found. I.	Found. II.
N	13.95	13.8	14.1

3,5-Dinitrobenzoylorthotoluidide, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ONHC_6H_4\overset{1}{C}H_3$.—This was purified for analysis by crystallizing from alcohol. It melted at 241°–242°. Analysis (Kjeldahl):

	Calculated for $C_{14}H_{11}O_5N_3$.	Found.
N	13.95	14.2

BY WALTER C. CHALKER.

3,5-Dinitrobenzoylmethylanilide, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ON(CH_3)C_6H_5$.—This derivative deposited from alcohol in prismatic crystals that melted at 155°–156°, without effervescence, to a clear oil. Analysis (Kjeldahl):

	Calculated for $C_{14}H_{11}O_5N_3$.	Found.
N	13.95	14.1

3,5-Dinitrobenzoyldiphenylamine, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ON(C_6H_5)_2$.—This compound was soluble in warm alcohol. It deposited,

[1] Behrend and Heymann: J. prakt. Chem., [2], **69**, 455.

on cooling, in prisms that melted, at 180°–181°, to an oil. Analysis (Kjeldahl):

	Calculated for $C_{19}H_{18}O_5N_2$.	Found.
N	11.57	11.8

3,5-Dinitrobenzoyl-α-naphthalide, $(\overset{3,5}{NO_2})_2C_6H_3\overset{1}{C}ONHC_{10}H_7$.—This compound was extremely insoluble in water and the ordinary organic solvents. It melted, at 268°, to a clear oil. Analysis (Kjeldahl):

	Calculated for $C_{17}H_{11}O_5N_3$.	Found.
N	12.46	12.50

NEW HAVEN, CONN.,
June 15, 1906.

SOME CONSTITUENTS OF THE POISON IVY PLANT.[1]

BY S. F. ACREE AND W. A. SYME.

Rhus Toxicodendron.

Up to the present time only three important chemical investigations of the poison ivy plant have been recorded, namely, those of Khittel,[2] Maisch,[3] and Pfaff.[4] The object of their work was to obtain the poisonous principle of the plant, and their results may be briefly stated as follows: Khittel thought that the poison was a volatile alkaloid, but he did not prove by physiological evidence that he had obtained a toxic substance. Maisch obtained a volatile acid, which he called *toxicodendric acid,* by distilling an aqueous extract of the plant. His acid was similar to formic and acetic acids, but more like the latter. He produced physiological evidence, of a doubtful character, to show that it was poisonous. Pfaff showed that the volatile acid of Maisch was probably impure acetic acid, containing traces of the poisonous substance which he thought

[1] This paper is an abstract of a dissertation submitted to the Board of University Studies of the Johns Hopkins University by W. A. Syme, for the degree of Doctor of Philosophy. A more detailed account of the work will be found in the dissertation.

[2] Amer. J. Pharm., 1858, 542.

[3] Proc. Amer. Pharm. Assn., 1865, 166. Amer. J. Pharm., 1866, 4.

[4] J. Expt. Med., **2**, 181 (1897).

was not volatile. He got from the plant a non-volatile oil, *toxicodendrol*, which he showed, by most reliable tests upon himself, to be the poison, or to contain it.

The present investigation was undertaken to see if more light could be thrown on the chemical nature of toxicodendrol. Soon after commencing work, however, it became apparent that the poison could be more intelligently studied if the substances associated with it in the plant were first identified. The scope of the work was, therefore, extended to an investigation of these other constituents.

The crude material for our work was prepared by Messrs. Parke, Davis and Company, of Detroit, Michigan, according to special instructions submitted to them: Fresh leaves and flowers of poison ivy were collected near Detroit and carefully inspected by a competent botanist. This material, which weighed 67.5 lbs., was completely macerated and put into 10 liter bottles, with ether. The mass was thoroughly shaken, water being added to make it more mobile. The ether was then separated and the extraction was repeated three times in the same way, to insure complete removal of the toxicodendrol. The ether extracts were combined, thoroughly dried with anhydrous sodium sulphate, and the ether was distilled off, the temperature being kept below 40° during the entire distillation. The residue, after the removal of the ether, was a thick, black, tar-like mass, weighing 3 lbs. 11 oz. In extracting the plant, about 24 gallons of ether were used. It is a significant fact, in regard to the volatility of the poison, that during the process of preparing this material, none of the employees engaged in the work were in any way affected, since proper precautions were taken and the utensils were handled with rubber gloves.

The crude ether extract, which will be designated as the "*original material*," was shipped to Baltimore in August and was kept in a cool place until November, when the investigation was begun. When the bottle was opened by the junior author there appeared to be an escape of vapor, and a nauseating odor suggesting crushed green leaves pervaded the atmosphere. Some days later irregular red patches appeared on his

face, though a mask of cotton cloth was worn during the work, and his hands were protected by rubber gloves.

The first experiment was to try to distil out the toxicodendrol from the original material with the aid of a vacuum pump. At a temperature of 140°–150° (2 mm.), the material carbonized and nothing passed over.

It was then thought that perhaps the oil could be converted into an ester which might be more volatile and could be distilled. Twenty grams of the original material were dissolved in 100 cc. of absolute alcohol, containing 3 grams of hydrochloric acid gas, and the mixture was heated 10 hours on a water-bath, under a return condenser. After the heating, the mixture had a delightful ethereal odor. The flask was closed and left standing several weeks, while other work was in progress. The ester solution was then put in a vacuum desiccator, over sulphuric acid, and the alcohol evaporated. A black, tarry, solid mass was left having the ester odor. It was extracted with warm water and filtered from insoluble tar. The filtrate was green and had the ethereal odor. It was shaken out with ether; the ether layer was blood-red and the aqueous portion deep green. The extraction with ether was continued until the water layer was no longer green. The combined ether extracts were evaporated in a desiccator, without heat. A black, tar-like solid was left, very much like the original material, but it had the ester odor. It was partly soluble in water and readily dissolved in alcohol. The alcoholic solution was tested on the skin and found not to be poisonous. The ester, or mixture of esters, was not investigated further in this connection, but was later shown to give the reactions for gallic acid and methyl furfuraldehyde. These reactions will be referred to in connection with other experiments.

Further preliminary work showed that the original mixture was very complex and that it would be necessary to fractionate it and examine the fractions separately. Chlorophyll could not be removed because the solvents for chlorophyll, *viz.*, alcohol, ether, carbon bisulphide, etc., dissolve large quantities of the mixture.

Some of the original material was extracted with 50 per cent

alcohol, filtered from insoluble tar, and the following experiments were performed with the filtrate *F*.

(1) A portion was distilled under diminished pressure and a yellow, acid liquid was obtained. This was shaken with ether and the latter evaporated. A small quantity of a yellow solid was left. The substance was not volatile enough to justify the use of this method for getting it.

(2) A precipitate obtained by adding lead acetate, in 50 per cent alcohol, to a portion of the filtrate F, was suspended in water, decomposed by hydrogen sulphide, shaken with ether, and the ether evaporated. The residue, after drying in a desiccator, was a yellow solid, apparently the same as that obtained by distillation in (1) above.

(3) Another portion of the alcoholic filtrate F was filtered through bone-black. The colorless filtrate was, apparently, pure alcohol and water, everything in solution having been removed by the bone-black.

In precipitating an alcoholic solution of the crude material with a solution of lead acetate, it was noticed that at least two kinds of precipitates were formed. The part deposited first was darker in color than that thrown down later. Pfaff used the last fractions in obtaining his oil, and stated that these precipitates consisted of the lead compound of the oil in a pure state. The authors found, by experiment, that the darker part was soluble in ether while the lighter portion was not. This indicated that the former consisted of tarry matter which was brought down mechanically, or which separated out when the alcoholic solution was diluted by the lead acetate solution, or that possibly it was a lead compound soluble in ether. To test this point an experiment was made as follows: Some of the crude material was thoroughly extracted with 50 per cent alcohol. The insoluble tar was then treated with 95 per cent alcohol, when most of it dissolved; the solution was filtered and lead acetate, in 50 per cent alcohol, was added. A greenish-colored precipitate was formed which was filtered off and found to be completely soluble in ether and soluble, to a considerable extent, in strong alcohol. These experiments suggested that the light-colored lead compound, which was thought to con-

tain the poison, could be purified by extraction with ether in a Soxhlet apparatus more conveniently than by the tedious process of fractional precipitation. Further preliminary experiments showed that 50 per cent alcohol extracted from the original material all of the substance or substances which gave the light-colored precipitate and dissolved only a small amount of the tar.

Some of the original material (288 grams) was then extracted several times with 50 per cent alcohol and filtered; the insoluble tar was washed and saved for examination. To the filtrate was added an excess of a solution of lead acetate, in 50 per cent alcohol. The large precipitate, which will be designated as "*Precipitate A*," was filtered and drained by suction in a Büchner funnel. The alcoholic "*Filtrate A*" was saved. *Precipitate A* was extracted with ether in Soxhlet extractors until the ether came over practically colorless, the operation being interrupted from time to time to stir up the precipitate in the thimble. The green-colored ether solution was saved for future examination. The lead precipitate, after being extracted with ether and dried, weighed about 116 grams. A portion of this lead compound was decomposed by hydrogen sulphide in a mixture of water and ether, which was well shaken during the operation. The ether was separated, filtered and evaporated under diminished pressure, without heat, there remained a yellow, oily residue having a pleasant odor. When the ether and water were completely removed in a vacuum desiccator, a hard, brittle, yellow resin, weighing about 16 grams, was obtained. It was soluble in alcohol, had a strong acid reaction and was free from nitrogen[1] and sulphur. The tests for nitrogen were made by the Lassaign and soda lime methods; this element was found very readily by means of soda lime in the tar left after extracting the original material with 50 per cent alcohol, but was not found by the Lassaign test. Sulphur was detected by means of sodium nitroprusside, after fusing the residue with sodium. The main portion of the lead compound was decomposed under alcohol, by hydrogen sulphide, filtered and the alcoholic filtrate evapo-

[1] Amer. J. Pharm., 77, 255 (1905).

rated *in vacuo*. The same yellow, acid resin was obtained. Experiments continuing through several weeks were made in applying solutions of this resin to rats, rabbits and guinea pigs. Finding it to be without effect upon these animals it was tried on the junior author and found not to be poisonous. Whenever it is stated in this paper that a solution was poisonous or not poisonous, the test was made by the junior author upon himself.

Gallic Acid.

An alcoholic solution of the resin was just neutralized with potassium hydroxide. During the titration the solution rapidly became dark brown. After neutralization it was shaken with ether; the water solution remained brown while the ether layer was nearly colorless and contained practically no dissolved substance. A portion of the water solution of the potassium salt, on being acidified with sulphuric acid and allowed to stand over night, deposited a slight precipitate with lead acetate, somewhat similar to the original lead precipitate *A*, and also slight precipitates with salts of zinc, mercury, copper and silver (with reduction). It gave a bluish-black color with impure ferrous sulphate and a dark color with ferric chloride. It reduced ammoniacal silver nitrate and Fehling's solution. These experiments indicated the presence of a tannin compound. An alcoholic solution of the resin gave the same color reactions with iron salts as did the potassium salt.

Further tests with a solution of the resin in dilute alcohol, and with an aqueous solution of the acid precipitated by adding sulphuric acid to a solution of the resin in potassium hydroxide, led to the conclusion that the acid is gallic acid. These tests were the following:

(1) Boiling with an excess of potassium hydroxide gave a black substance, tauromelanic acid.

(2) The acid was not precipitated by gelatin.

(3) On the addition of potassium cyanide a transitory, red color was produced, which reappeared on shaking with air.

Gallic acid is distinguished from tannic acid by tests 2 and 3.

At later stages in the work the potassium, barium and

sodium salts of gallic acid were obtained and, finally, the pure acid was made by decomposing the sodium salt with sulphuric acid and crystallizing from water. The melting point of the acid corresponds with that of gallic acid; it melted, with decomposition, at about 230°.

For further identification, some of the acid was converted into the ethyl ester by the method of Grimaux.[1] The ester obtained agreed in melting point and other properties with that described by Grimaux. The same compound was also made from gallic acid from another source and the esters agreed in properties. A mixture of the two specimens melted within the limits given for the ethyl ester of gallic acid, 156°–159°.

While the tests leading to the identification of gallic acid were being made, another series of experiments was in progress. Eleven and one-half grams of the resin obtained from lead precipitate *A*, by decomposition with hydrogen sulphide, were treated with 0.1 N potassium hydroxide, added from a burette until the acid was exactly neutralized. All went into solution. On shaking with ether, some of the potassium salt separated out and was saved for examination. The solution became dark brown on exposure to the air and got darker as the work proceeded. The acid in solution as a potassium salt was precipitated out in 4 fractions, by adding one-fourth the amount of 0.1 N sulphuric acid required to neutralize the potassium hydroxide used.

The precipitates were filtered off and examined. The first was small in amount, gummy and difficult to filter. The solution was shaken with ether after each precipitate had been filtered off. The succeeding precipitates were in better condition, but were not pure. All appeared to be impure gallic acid, which had become brown by absorption of oxygen, but they were saved to be tested for poison. After the last fraction had separated the filtrate was shaken several times with ether and retained for further examination, which will be described under "rhamnose." This filtrate is designated as *B*.

A portion of the resin obtained from lead precipitate *A* was tested and found not to be poisonous, as already mentioned.

[1] Bull. Soc. Chim., [2], 2, 95 (1864).

By this test, all the substances contained in the lead precipitate *A*, after its extraction with ether in the Soxhlet apparatus, were eliminated from the possible poisonous substances. The poison must, therefore, have been extracted by the ether.

A portion of the original poisonous material was treated with 50 per cent alcohol and filtered from insoluble tar. The filtrate was precipitated in 6 fractions by lead acetate. The last fractions were lighter in color and, apparently, much purer than the first. The sixth lead precipitate was decomposed by hydrogen sulphide. The light yellow, aqueous solution was tested and found not to be poisonous. It gave the characteristic reactions for gallic acid. The poison, if precipitated at all by lead acetate, must have been contained in one of the preceding fractions. Later experiments showed that it is brought down, partly mechanically and partly as a lead compound, in the first precipitation.

Fisetin.

Some of the original material was extracted with hot water to remove gallic acid and filtered from tar while hot. The filtrate had a deep yellow color. On cooling over night, an olive green precipitate separated out which, when dry, was a light powder. It was practically insoluble in cold water, but soluble with great difficulty in boiling water, from which it separated in yellow flakes; it dissolved slightly in ether and acetic acid and readily in alcohol. The solutions, which were not acid to litmus, gave a dark color with ferric chloride, an orange red precipitate with lead acetate, which was easily soluble in acetic acid, and an orange yellow precipitate with stannous chloride. These properties and reactions indicated that the substance was the dye-stuff fisetin and that it occurs in the free state in this plant, though it is usually found as a glucoside of fisetin combined with tannic acid.

The substance which separated from the boiling water solution was further purified by dissolving it in a small quantity of hot alcohol and adding hot water. On cooling, the yellow compound separated out in a flocculent condition. Examined under a microscope, the flakes appeared to be made up of

masses of fine crystals. The substance was found to have the characteristic properties of fisetin described by Schmid,[1] and on fusion with potassium hydroxide[2] gave protocatechuic acid and phloroglucinol. These substances were identified by characteristic tests.

Rhamnose.

Schmid[3] obtained a sugar solution by the decomposition of a fisetin glucoside from *Rhus cotinus*, and Perkin[4] obtained the same from a glucoside in *Rhus rhodanthema*. They thought that the sugar in both cases was isodulcite, but they did not isolate it. Assuming that the free fisetin found in *Rhus toxicodendron* had its origin in the decomposition of a fisetin glucoside by natural processes, it was reasonable to suppose that the sugar would also be found in the free state, although, with one or two possible exceptions,[5] rhamnose has not been found except as a glucoside body.

Since rhamnose forms a lead compound, the sugar, if present, should be found in the first lead precipitate, *A*, and also in the filtrate *A* in case it is not completely precipitated in the presence of acetic acid and alcohol.

About 2 liters of the filtrate *A* were examined first. It had a light yellow color, contained an excess of lead acetate and was acid from the acetic acid liberated in the precipitation of the lead compound *A*. This filtrate was evaporated to dryness, under diminished pressure, to remove alcohol, water and acetic acid. The clear distillate had a peculiar odor suggesting both tea and amyl formate. It was saved for examination and was found to be not poisonous. The residue in the dish, after evaporation, was a tough, reddish brown, gummy mass which could be drawn out into fine threads. It had a pleasant, sweet odor. It was extracted several times with hot water, each portion being filtered. A yellow brown powder remained undissolved and was saved. The combined filtrates deposited more of the yellow solid on standing. The filtered liquid was

[1] Ber. d. chem. Ges., **19**, 1740.
[2] *Ibid.*, **19**, 1747; Ann. Chem. (Liebig), **113**, 97.
[3] *Loc. cit.*, **19**, 1738.
[4] J. Chem. Soc., **71**, 1194.
[5] Chem. Ztg., **23**, Rep., 177.

freed from lead by hydrogen sulphide. The solution then had a lemon yellow color, a sweet odor and was acid from acetic acid. On concentrating the solution by evaporation and making a small portion of it alkaline with sodium hydroxide, the yellow color came out very intensely by warming with alkalies or barium hydroxide.[1] Rhamnose is colored yellow under these conditions. The alkaline solution reduced Fehling's solution and ammoniacal silver nitrate, indicating the presence of a sugar. Another portion of the solution gave a slight precipitate with phenylhydrazine, in the cold. The remainder of the solution was evaporated to dryness, extracted with water, filtered and again evaporated. A dark, sticky syrup was left which was only partly soluble in water. This was treated with water, filtered and the filtrate evaporated, the water being replaced from time to time to remove acetic acid. Finally, the liquid gave the following tests for rhamnose, besides those already mentioned:

(1) With α-naphthol[2] and sulphuric acid, a purple violet color.

(2) With thymol[2] and sulphuric acid, a red color.

(3) With resorcinol[3] and sulphuric acid, a red color.

(4) With orcinol[4] and hydrochloric acid, a red color.

(5) With ammonium picrate and sodium picrate, a yellowish red color.

(6) With phloroglucinol and hydrochloric acid, a red color.

(7) It decolorized an alkaline solution of potassium ferricyanide.

(8) It gave a white precipitate with lead acetate.

The filtrate *B* (p. 307), from which gallic acid was precipitated by sulphuric acid in 4 fractions, was saved to be examined for sugar. To remove gallic acid completely, and other vegetable matter, it was shaken out several times with ether and was kept at a low temperature with salt and ice for a long time. It was left standing for several weeks, during the course of which more brown matter separated and was filtered off.

[1] Chem. der Zuck., I, 177.
[2] *Ibid.*, I, 188.
[3] Rayman: Bull. Soc. Chim., 47, 668 (1887).
[4] Acides Gummiques, Garros.

The filtrate was evaporated to a small bulk, cooled and filtered from crystals of potassium sulphate. The filtrate was evaporated to dryness, the residue taken up in water and filtered through bone-black. Addition of alcohol caused complete precipitation of potassium sulphate. The solution then gave the above-mentioned, characteristic tests for rhamnose.

All attempts to get the osazone of the sugar by Fisher's method failed, probably on account of the small quantity of sugar present. The plant, it will be remembered, was originally extracted with ether, in which rhamnose is practically insoluble. The tests above described, however, can leave no doubt as to the identity of the sugar.

Additional evidence that the sugar is rhamnose was obtained by a method for testing for the presence of this sugar described by Maquenne.[1] This consists in converting the sugar into methyl furfuraldehyde, by distilling the substance to be tested with dilute sulphuric acid. The presence of methyl furfuraldehyde in the distillate is shown by a green color with alcohol and sulphuric acid. "This procedure is applicable to extracts as well as to entire plants, and has the advantage that it does not require the separation of isodulcite, the crystallization of which is often very slow, and at times impossible, when it is mixed with other very soluble substances."[2]

The experiment was tried with the crude ether extract of the plant, according to the directions of Maquenne, and the green color with alcohol and sulphuric acid was obtained from the thicker, oily portion of the distillate. This test can be made with hydrochloric acid[3] as well as with sulphuric. Therefore, the color test was tried with the ester mixture prepared in one of the early experiments by boiling the original plant material with hydrochloric acid and alcohol. Methyl furfuraldehyde was found here also, indeed better results were obtained than by following Maquenne.

The presence of free rhamnose has thus been shown in the original material, in the first precipitate by lead acetate and in the filtrate from this precipitate. Experiments to be described

[1] Ann. Chim. Phys. [6], **22**, 93 (1891).
[2] *Loc. cit.*
[3] Biochem. der Pflan., I., 210.

under "*The Poison*" showed that the ether extract from the Soxhlet apparatus contained a substance which yielded rhamnose when hydrolyzed by dilute sulphuric acid.

The presence of free gallic acid, fisetin and rhamnose in the plant can be readily explained by a series of assumptions for which there is a considerable amount of experimental evidence. There is reason to believe that tannin-like bodies are formed at the expense of chlorophyll,[1] that complex tannin compounds can be broken down by acetic acid, which is also found in *Rhus toxicodendron*, into a tannic acid and a glucoside; for example, "fustin-tannide"[2] yields tannic acid and fisetin glucoside; and, finally, that the glucoside can be hydrolyzed by acids or enzymes giving, in the sumach plants, fisetin and rhamnose.

Nitrogenous ferments which can effect the hydrolysis of glucosides and give rise to sugars are frequently found in plants, for example, emulsin in almonds, myrosin in mustard, and erythrozym in madder. Acree and Hinkins[3] found that diastase, pancreatin and a number of other enzymes cause the hydrolysis of triacetyl glucose with the formation of glucose and acetic acid. Stevens[4] obtained a nitrogenous oxidizing enzyme from *Rhus vernicifera*. The close relationship between the poisonous species of *Rhus* would lead us to suppose that the same soluble ferment exists in poison ivy, though it was not detected in the original material used in these experiments, probably because the plant was extracted with ether in which the enzyme is insoluble. The existence of such a soluble ferment would explain the presence of free sugar and free fisetin.

The Poison.

Some of the original poisonous material (288 grams) was extracted with 50 per cent alcohol, and this alcoholic solution was precipitated with lead acetate in the manner already described (p. 304). The lead precipitate so obtained was extracted with ether in Soxhlet extractors and, after the extraction, was found by test to be free from poison. Therefore, the poison, if precipitated by the lead acetate, must have been ex-

[1] Compt. rend., **113**, 892.
[2] Schmid: Ber. d. chem. Ges., **19**, 1736.
[3] THIS JOURNAL, **28**, 370.
[4] Amer. J. Pharm., **77**, 255 (1905); **78**, 53 (1906).

tracted by the ether. This ether solution had a dark green color, and was acid from acetic acid brought down in the lead precipitate. The ether was evaporated in a vacuum desiccator without heat and there remained a small quantity of an acid mixture of water and a soft tar; the watery part was colored green, showing that the tar was soluble to some extent in dilute acetic acid. The mixture had the peculiar odor of the original material. A small drop of the green, watery part was applied to the wrist, allowed to remain a few minutes and was then removed by absorbent paper, but the spot was not washed. Itching and reddening of the skin commenced within 24 hours. At the end of 48 hours there was a well-developed case of poisoning. This was cured by immersing the arm in a hot solution of potassium permanganate.

A small portion of the poisonous mixture was dissolved in alcohol, and this solution was divided into 3 parts. The first part was treated with ferric chloride, but it gave no color reaction. Another portion of the alcoholic solution was diluted with water; it became turbid. The third portion gave a dirty green precipitate with lead acetate, which seemed to come down more readily when the solution was diluted with water. The main portion of the poisonous mixture was then dissolved in 95 per cent alcohol and lead acetate, in 50 per cent alcohol, was added. The precipitate was filtered, washed and decomposed by hydrogen sulphide, in a mixture of water and ether. The ether solution was filtered and evaporated. The residue was a tar which, on standing in a desiccator for some time, became dry enough to be broken into sticky lumps. An alcoholic solution of this substance gave a dark color with ferric chloride and a light colored precipitate with lead acetate.

To get more of the poisonous tar for study, 233 grams of original material were extracted with 95 per cent alcohol. Strong alcohol was used in order to dissolve as much of the tar as possible. The solution had a dark, greenish color but was somewhat yellow in thin layers. The undissolved tar was filtered off and extracted twice again in the same way. The tar left after the third extraction was only slightly soluble in alcohol, and its solution was not poisonous. The 3 filtrates

from these 3 extractions were precipitated separately by lead acetate, in 50 per cent alcohol. The first precipitate was largest, darkest in color and carried down the most tarry matter. The second was light green. The third, which was quite small, was black and was not a lead compound at all, but some of the tar which separated out on diluting the strong alcohol with the weaker containing lead acetate. It was soluble in ether and less soluble in alcohol. The alcoholic solution of this third portion gave no precipitate with hydrogen sulphide. The first and second lead precipitates were filtered by suction and washed with water. They were kept a day or two in a desiccator over sulphuric acid, but did not become completely dry. The weight of these two moist precipitates together was 172 grams. They were combined and extracted with ether in Soxhlet extractors, which were kept in operation during work hours for 3 days.

In the meantime the alcoholic filtrates from these lead precipitates were combined and concentrated on the water-bath, by distilling off 2 liters of alcohol. The alcohol obtained had the peculiar odor of the original material, but was not poisonous.

After a long extraction of the lead precipitate in the Soxhlet extractors, the green, ether solutions were combined and washed by shaking them with water, to remove lead acetate and acetic acid, in case any should have been held in the lead precipitate. The ether was distilled off at a low temperature and there remained a soft tar, a portion of which was not completely soluble in 95 per cent alcohol. The alcoholic solution had a greenish-yellow color and was poisonous. The tar was also partly soluble in acetic acid, and this solution was found to contain lead. Thinking that the lead acetate had not been completely washed out, the main part of the tar was dissolved in ether and shaken with water. The wash water continued to give a test for lead as long as the washing was continued. This indicated the probable hydrolysis of an unstable lead compound. To remove the lead, hydrogen sulphide was passed into the ether solution mixed with water. Lead sulphide was filtered off and the ether was evaporated. A small

portion of the tar residue, in alcoholic solution, gave a color reaction with ferric chloride. As this may have been due to traces of lead gallate dissolved in the extraction with ether and afterwards decomposed by hydrogen sulphide, the main portion of the tar was redissolved in ether and shaken with water until it no longer reacted with ferric chloride. The ether was then evaporated and a soft, black, poisonous tar or gum of uniform consistency was left, which was proved to be free from gallic acid and lead. These experiments showed that some of the poison was precipitated as a lead compound soluble in ether and some was brought down mechanically in the free state. To see if the extraction with ether in the Soxhlet apparatus was complete, the residue in the thimbles was decomposed by hydrogen sulphide and shaken with ether. The dark-colored, ether solution was freed from gallic acid by shaking with water and dilute sodium carbonate solution, and was evaporated. A small quantity of tar was obtained which was added to the main portion.

A solution of the poisonous tar in 95 per cent alcohol did not reduce Fehling's solution and did not give a precipitate with lead acetate, except for the separation of a small quantity of tar, which was not a lead compound. The lead compound of the poison was, apparently, soluble in 95 per cent alcohol as well as in ether, for it would not precipitate in this medium, although it was found in the original precipitate by lead acetate. The alcoholic solution of the tar became turbid on diluting with water.

A portion of the tar was distilled, under diminished pressure, with acetic acid, which is present in the plant. It was soluble to some extent in the acid. The temperature did not go higher than 55° during the distillation. A tube containing cotton, moistened with sweet oil, was placed between the receiver and the water suction, so that the uncondensed vapors would have to pass through the cotton. This cotton was rubbed on the skin and was not poisonous. The yellow distillate collected in the receiver was also tested and was not poisonous. This proves that the poison, after its removal from the plant, is not volatile with the vapor of acetic acid.

Hydrolysis of the Poison.

About 5 grams of the tar, free from gallic acid and sugar, were dissolved in alcohol and dilute, 2 per cent, sulphuric acid was added, which caused a separation of some of the tar. The mixture was heated on a water-bath during work hours, for 4 days. A purple and green fluorescent solution was formed, though much tar was left apparently unchanged. The alcohol was evaporated off and the solution filtered from tar. The fluorescent filtrate was shaken with ether, by which the green substance was removed, leaving the solution purple. The ether left, on evaporation, a small quantity of a green material having a pleasant, ester odor. It was not further examined. A portion of the purple solution was exactly neutralized with sodium carbonate. This liquid gave a blue-black color with ferric chloride, which became red on the addition of another drop of sodium carbonate, indicating the presence of gallic acid. It also reduced Fehling's solution.

Another portion of the purple solution was made alkaline with sodium carbonate. A reddish-brown, flocculent precipitate was formed and was filtered off. The filtrate did not give any color with ferric chloride, but it reduced Fehling's solution. It also gave the test for rhamnose with α-naphthol.

The main portion of the purple solution was made alkaline with sodium carbonate; the precipitate was filtered off and dissolved in acetic acid. The solution was yellow and gave a reaction with ferric chloride similar to that of gallic acid. The filtrate from the precipitate obtained with sodium carbonate was concentrated by evaporation until sodium sulphate began to crystallize out. Alcohol was added to precipitate this salt completely; the mixture was heated and filtered. The alcoholic filtrate was concentrated to a syrup which reduced Fehling's solution and gave the characteristic test for rhamnose already mentioned. By this hydrolysis, the tar was split up into rhamnose and some form of gallic acid which could be precipitated by sodium carbonate. The compound, whose acetic acid solution was yellow, probably also contained fisetin. This statement is based on the results of the experiment described in the next section.

Decomposition of the Poison with Acetic Acid.

A portion of the poisonous tar was heated in an open dish with strong acetic acid. The tar seemed to be decomposed to some extent, giving a yellow substance. Acetic acid was added from time to time as it evaporated. After several evaporations, water was added, the mixture was heated to boiling and filtered. This filtrate, "No. 1," will be mentioned later. The residue in the dish consisted of undecomposed tar and an olive green, flaky substance, which latter was heated with a fresh portion of glacial acetic acid. Water was added and the mixture was boiled and filtered. The filtrate had a deep yellow color, suggesting fisetin. It was shaken out with ethyl acetate, which became colored yellow. A portion of the ethyl acetate solution gave an orange red precipitate with lead acetate, showing the presence of fisetin. The ethyl acetate was removed from the remainder of the solution by evaporation and the yellow residue was taken up in alcohol. This alcoholic solution gave the characteristic reactions for fisetin with stannous chloride, potassium hydroxide, ferric chloride and Fehling's solution.

Filtrate No. 1, obtained by heating the poisonous tar with acetic acid and hot water, as described above, was investigated as follows: A portion of it gave a reddish-colored precipitate with sodium carbonate, as in the case when the tar was hydrolyzed with sulphuric acid. The remainder was nearly neutralized with sodium carbonate and lead acetate was added, in excess, to remove gallic acid. The excess of lead was precipitated with sulphuric acid, and the sulphuric acid removed by barium carbonate. The solution, on evaporation, reduced Fehling's solution to some extent, but a white precipitate was also formed.

In this experiment, gallic acid and fisetin, and probably sugar, were formed by the decomposition of the poisonous gum with acetic acid, the acid found in the plant by Pfaff. The presence of free gallic acid, fisetin and rhamnose in the plant can be explained by the natural hydrolysis of a complex gum or tar, or of a constituent thereof.

The poisonous property is lost in the general rearrangement which takes place during hydrolysis, but the poisonous tar was not hydrolyzed by boiling with a dilute solution of sodium carbonate.

It was found, as has been stated elsewhere, that the lead compound of the poison could not be precipitated in 95 per cent alcohol. Further experiments, however, showed that on extracting the poisonous gum with 50 per cent alcohol, a portion of it dissolved, and this solution gave a precipitate with lead acetate, which was a true lead compound. The remainder of the purified tar, about 10 grams, was treated with 50 per cent alcohol and filtered. Very little dissolved in alcohol of this strength, but on the addition to the solution of lead acetate, in 50 per cent alcohol, a light colored precipitate was formed, which became dark on standing. It was filtered off, washed free from lead acetate, decomposed by hydrogen sulphide and shaken out with ether. The ether left, on evaporation, a yellow, resinous substance having a faint odor like garlic. By drying in a desiccator, a small quantity of solid, yellow resin was obtained which was completely soluble in alcohol. A very small drop of this solution applied to the skin on the end of a glass rod, which had been drawn out to a point, caused an eruption in about 36 hours. Following the nomenclature used by Maisch and Pfaff, this substance will be designated as *Toxicodendrin*.

The filtrate from the lead precipitate just described was freed from the excess of lead acetate by means of hydrogen sulphide, and was found to be poisonous, showing that the precipitation by lead acetate was not complete even in 50 per cent alcohol. On spontaneous evaporation of the solution a yellow, sweet smelling resin was left.

A portion of the alcoholic solution of the toxicodendrin gave a dark coloration with ferric chloride, but did not reduce Fehling's solution and was slightly acid to litmus.

To see whether the toxicodendrin could be hydrolyzed, the remainder was dissolved in alcohol and dilute sulphuric acid was added. A fine, white precipitate was formed at once which, on standing, rose to the surface as a light, flocculent

substance. The mixture was heated for several days on a water-bath, filtered from unhydrolyzed resin and the filtrate neutralized and concentrated in the way already described. The solution obtained reduced Fehling's solution. Not enough was available for further sugar tests, but all the hydrolysis experiments point to the conclusion that the poisonous substance is a rhamnoside, and is the source of the sugar in the plant.

The reaction with ferric chloride, observed whenever a lead compound of the poison is decomposed by hydrogen sulphide, may be explained by the formation of traces of gallic acid or fisetin through the action of the weak acids present.

The supply of purified poisonous tar having been exhausted in the preceding experiments, further study of the active principle is postponed until more can be prepared. It is highly desirable to investigate the white precipitate formed by the addition of sulphuric acid to an alcoholic solution of the toxicodendrin.

Oxidation of the Poison with Nitric Acid.

When the purified poisonous material (p. 312) was extracted with 50 per cent alcohol only a small quantity was dissolved, as was stated above. The insoluble residue was treated with fuming nitric acid. A violent reaction took place at once, with a copious evolution of red fumes and heat. When the reaction was over, a sticky, red, gummy mass was left which was slightly soluble in cold water and readily soluble in warm alcohol. The water extract was yellow and the alcoholic solution red. That the water extract contained picric acid was shown by the following experiments:

(1) A portion was gently warmed with a few drops of a strong solution of potassium cyanide and 2 drops of sodium hydroxide. The red color of potassium isopurpurate was formed.

(2) A portion of the water solution was heated with glucose and a few drops of sodium hydroxide. The deep red color of picraminic acid was produced.

(3) A few drops of an ammoniacal solution of copper sul-

phate was added to the water extract. A yellow-green precipitate was formed.

(4) The water extract dyed silk, but did not dye cotton cloth.

Distillation of the Tar with Soda Lime.

About 25 grams of the tar, left after extracting the original material with hot water, was dissolved in ether and poured into a glass retort containing soda-lime. The ether was distilled, leaving the tar intimately mixed with the soda-lime. The retort was then gradually heated. Vapors and liquid were given off, both of which turned red litmus blue and had a strong odor like tobacco smoke. No odor of ammonia was detected.[1] At the high temperature of the triple burner, a semisolid, red, greasy substance collected in the condenser tube and closed it. This material had the same powerful odor as the liquid portion of the distillate. The clear, watery portion of the distillate was separated from the thicker parts, and was proved, by the following characteristic tests, to contain pyrrol and pyridine derivatives:

(1) Wood moistened by hydrochloric acid was turned red by it.

(2) Colorless fumes were formed when brought near hydrochloric acid. When mixed with hydrochloric acid, a red insoluble substance was formed.

(3) It precipitated the hydroxides of iron, gave a light blue precipitate with copper sulphate and a white precipitate with mercuric chloride.

The greasy, semisolid mass was extracted with 10 per cent hydrochloric acid and filtered. On the addition of a solution of mercuric chloride to the red filtrate a brown, flocculent precipitate was formed. It was filtered off and distilled with sodium hydroxide, but the distillate did not contain pyridine.

Summary.

Leaves and flowers of the poison ivy plant were extracted with ether and the ether was removed by evaporation. In the

[1] *Vide*, Amer. J. Pharm., 77, 256.

residue, the following substances were found and studied. Gallic acid, fisetin, rhamnose and a poisonous tar, gum or wax.

The lead compound of the poison was soluble in ether; which gives a means of separating the poisonous from the non-poisonous matter in one operation.

The poison was not volatile with the vapors of acetic acid or alcohol.

The poisonous tar or wax was decomposed by acids and yielded gallic acid, fisetin and rhamnose, showing the probable source of these compounds in the plants, and indicating that the poison is a complex substance of a glucoside nature.

It was found that a portion of the poisonous material could be precipitated by lead acetate from a solution of the purified tar in 50 per cent alcohol.

All cases of poisoning developed on the junior author were easily cured with potassium permanganate.

The following method is suggested for obtaining the poisonous substance from the plant. Extract the plant with alcohol, filter and precipitate at once with lead acetate. Wash the precipitate, dry and extract it with ether in loosely filled Soxhlet extractors. Combine the ether extracts, mix with water and pass in hydrogen sulphide. Separate the water and the ether solution, and filter the latter. Wash the ether solution thoroughly by shaking with water, and then evaporate at a low temperature.

JOHNS HOPKINS UNIVERSITY,
June 1, 1906.

OBITUARY.

RUDOLF KNIETSCH.

Dr. Rudolf Knietsch died at Ludwigshafen on May 28, 1906. The whole of his active career was passed in the service of the "Badische Anilin-und Soda-Fabrik," which he entered exactly 22 years before the date of his death. During this period Knietsch had won for himself one of the foremost places in the ranks of technological chemists. We owe it to him that liquid chlorine became an article of commerce. His researches, carried on during 10 years, resulted in the applica-

tion of the "contact process" to the manufacture of concentrated and dilute sulphuric acid, and he took an active share in the technical synthesis of indigo. In 1904 the Verein deutscher Chemiker conferred on Knietsch the "Liebig" gold medal.

REVIEWS.

THE CYANIDE INDUSTRY PRACTICALLY AND THEORETICALLY CONSIDERED. By R. ROBINE and M. LENGLIN, translated by J. ARTHUR LECLERC, PH.D., with an appendix by C. E. MUNROE, PH.D. First edition. London: Chapman & Hall; New York: John Wiley & Sons. 1906. pp. 408. Price, $4.00.

The authors offer, in this book, a complete description of the chemistry of cyanogen and its derivatives from chemical and industrial points of view. In Part I. a description of the individual cyanogen derivatives is followed by a study of their analytical properties, of methods of analysis, of toxicological methods and of thermochemical data; these last are quoted from Berthelot.

The processes for manufacturing cyanides are classified as non-synthetic and synthetic; the first class includes 10 patented processes for extracting cyanides from sulphocyanides. The authors describe 28 synthetic processes, utilizing atmospheric nitrogen, 24 utilizing ammonia and several special processes besides. The manufacture of ferrocyanides, ferricyanides, sulphocyanides and Prussian blue are described with equal fulness. An appendix by Dr. Munroe, containing a study of the use of cyanides for the extraction of precious metals from their ores and a descriptive list of the U. S. patents on the subject, closes the book.

While the authors describe historically so many patented processes, they discriminate clearly between those which have present or prospective value and those which are technically valueless; their criticisms on the different processes are very interesting and show a thorough knowledge of the subject.

The following are some of the more important and successful cyanide processes. Rossler and Harlacher's, which depends on this reaction, fused

$$K_4Fe(CN)_6 + 2Na = Fe + 4KCN + 2NaCN.$$

Playfair's, by fusing sulphocyanide with zinc,

$$KCNS + Zn = ZnS + KCN.$$

Frank and Caro's process and those of Dziuks and of the General Electric Chemical Co., all depending on the action of

atmospheric nitrogen on carbides. That of the Stassfurter Chemische Fabrik, depending on the interaction of ammonia, heated charcoal and alkali, and said, by the inventors, to occur in the following stages: At dull red heat,

$$2C + 2NH_3 + 2KOH = KCN + KCNO + H_2O + 3H_2;$$

on increasing the heat the cyanate is reduced to cyanide by the carbon. Castner's famous method, utilizing ammonia and sodium; in the first stage of this process sodamide is made, $NH_3 + Na = NH_2Na + H$; the fused sodamide is then treated with heated charcoal, forming cyanide—$NH_2Na + C = NaCN + H_2$. The process of the Deutsche Gold und Silber Scheide Anstalt, which combines the advantages of the processes of Frank and of Castner. Ammonia is conducted over a mixture of fused sodium and charcoal at 400°, forming sodamide, which at this temperature reacts with carbon, yielding sodium cyanamide, $2NaNH_2 + C = CNNa_2 + 2H_2$. On raising the temperature to 800°, $CNNa_2 + C = 2NaCN$; the yield is said to be nearly the theoretical.

Space considerations forbid reference to further processes, although those for obtaining ferrocyanide from the residues in the purification of coal gas are of great interest. Enough has been said to show that the book is one of definite value to chemists. Dr. LeClerc has made an excellent translation and the book is well printed and illustrated. E. R.

URIC ACID. The Chemistry, Physiology and Pathology of Uric Acid and the Physiologically Important Purin Bodies, with a Discussion of the Metabolism in Gout. By FRANCIS H. MCCRUDDEN. New York: Paul B. Hoeber: 1905. pp. 318. Price, paper $2.50; canvas, $3.00 net.

The author here presents the uric acid problem in all of its phases. In dealing with the chemistry of uric acid he begins with its discovery by Scheele, in 1776, and recounts briefly the history of the subject, including the contributions of Liebig and Wöhler, Baeyer, Horbaczewski, Behrend and Fischer. The recent brilliant contributions of physiological chemistry on the synthesis and decomposition of uric acid in birds and mammals are considered in detail. The book includes a consideration of the effect of exercise, diet and drugs on the formation and excretion of uric acid, special stress being laid on those drugs which are used clinically in the treatment of gout. The pharmacological action of the purin derivatives is also discussed. The work of the author in collecting this large amount of widely-scattered literature has been excellently done and the presentation is clear and concise. The admirable bibliography is also a feature of the volume. The

book will be of value to all who are interested in medicine and the medical sciences. A. S. L.

PHYSICAL CHEMISTRY FOR ELECTRICAL ENGINEERS. By J. L. R. MORGAN, PH.D., Professor of Physical Chemistry in Columbia University. New York: John Wiley & Sons. 1906. Price, $1.50.

This small book of 230 pages consists of 8 chapters, as follows: Some Fundamental Principles; The General Properties of Gases; Heat and Its Transformation into Other Forms of Energy; Solutions; Chemical Mechanics; Equilibrium in Electrolytes; Electrochemistry; Problems.

In Chapter I. the author insists on the necessity of distinguishing clearly between fact and hypothesis in the matter of atomic and molecular weights, especially at the present time, and to avoid confusion of this character he proposes, throughout the book, to relinquish hypothesis and consider only facts and their generalization. The last chapter consists of a list of 78 problems taken from the author's "Elements of Physical Chemistry." The remaining chapters contain the material presented to the student, the one on electrochemistry being, naturally, much more elaborate than the others.

The book is not intended to be a text-book, its aim is to equip students with the knowledge necessary to understand the current literature in the field of electrochemistry, a branch of science which the author feels has been neglected in their teachings by both physicists and chemists.

The book is clearly written and, on the whole, free from errors, except such minor ones as would be noticeable only to one actively engaged in the particular field treated. The author has made a wise choice of material, but could not the desired end have been reached more satisfactorily by a short treatise on physical chemistry, where the subject would appear in its proper relation to other branches of the science?

J. C. W. F.

THIRD TREATISE ON THE EFFECTS OF BORAX AND BORIC ACID ON THE HUMAN SYSTEM. Being a Critical Review of the Report of DR. H. W. WILEY, Chief of the Bureau of Chemistry of the U. S. Department of Agriculture. By DR. OSCAR LIEBREICH, o. o. Professor der Universität Berlin und Geheimer Medizinalrat. (Translated from the German.) London: J. & A. Churchill. 1906. pp. 70. Price, $1.75 net.

As stated on the title page, this treatise is merely a critical review of Bulletin No. 84, by Dr. H. W. Wiley. It contains no new data or facts and, therefore, it is only possible to call attention to the book and reserve any remarks until more experimental work is done. A. S. L.